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Surgery, Gynecology and Obstetrics

WITH

International Abstract of Surgery

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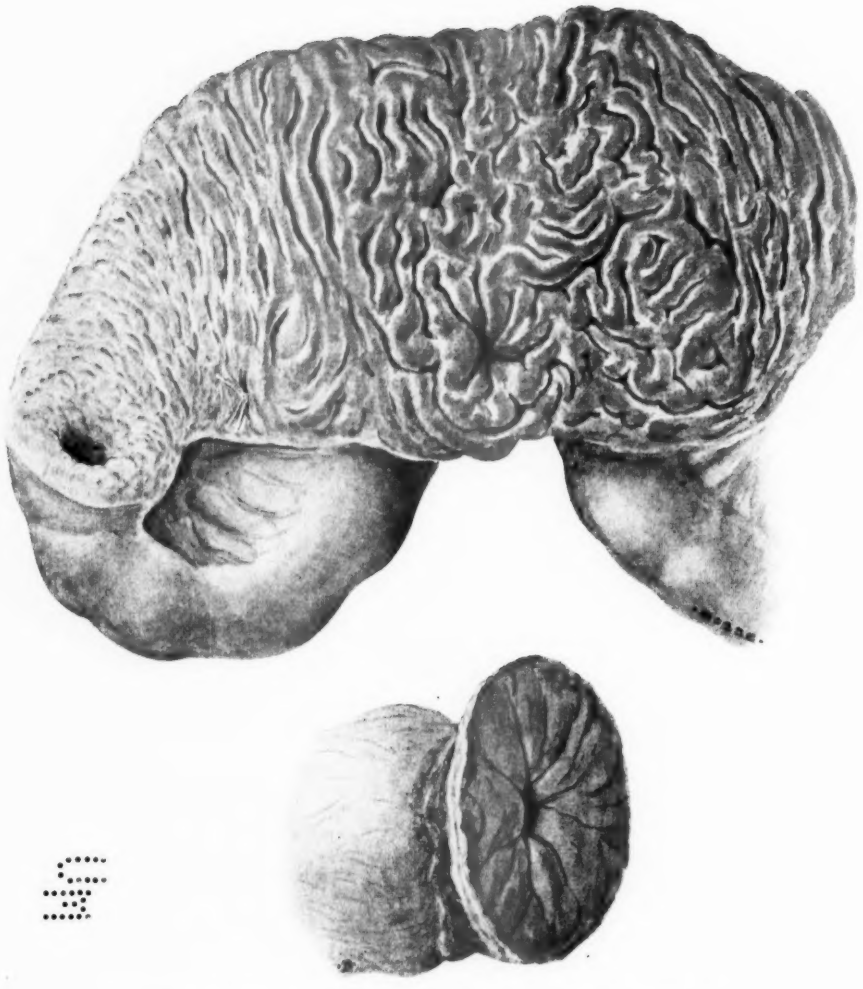

Fig. 6 (above). Stomach of Dog 246, 87 days after Biondi operation.
Fig. 8. Resected pylorus (patient B. C.). Stitch still in place, 20 months after pyloric exclusion. Pylorus patent.

(*Richard Lewisohn.*)

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PYLORIC EXCLUSION

AN EXPERIMENTAL AND CLINICAL STUDY[1]

BY RICHARD LEWISOHN, M.D., NEW YORK CITY

UNTIL a few years ago gastro-enterostomy was generally considered the method of choice for the treatment of pyloric and duodenal ulcers. It was considered unnecessary to add anything to this procedure. Even in the recent literature we find papers advocating this operation for ulcers of the stomach and duodenum. Paterson, for instance, read a paper before the Clinical Congress of Surgeons, in Chicago, two years ago, in which he stated that "the occlusion of the pylorus is an unnecessary complication of gastrojejunostomy and is based on erroneous pathology."

This opinion, however, is rather an isolated one. In fact most surgeons agree that a simple gastrojejunostomy will not permanently cure the disease. Those who advocated simple gastro-enterostomy for the cure of pyloric and duodenal ulcers, assumed that all the food with the gastric juices would pass directly through the anastomosis between stomach and jejunum, and no longer through the pylorus and duodenum.

Kelling, however, proved conclusively about fifteen years ago the fallacy of this idea. He established a gastrojejunostomy and a duodenal fistula in dogs, and observed that most of the stomach contents were discharged through the duodenal fistula and that only a small amount of food passed through the anastomosis into the intestines. It is thus clear that a simple gastro-enterostomy will not prevent the food from passing over the ulcerated area. To be sure, the regurgitation of bile through the anastomosis probably plays a certain curative rôle, by counteracting the hyperacidity of the stomach contents. This alkalinization alone, however, does not suffice to cure ulcers permanently.

Furthermore, it is a well-known fact that without simultaneous resection or occlusion of the pylorus a simple gastro-enterostomy is apt to contract in a very short time. Thus all the food will again pass through the pylorus and conditions which existed before the operation, will be re-established.

The vast majority of surgeons, therefore, agree that pyloric exclusion ought to be added to gastrojejunostomy to insure the permanent cure of pyloric and duodenal ulcers. This consensus of opinion, however, holds good only for the principle of pyloric exclusion. There still exists a great difference of opinion as to the best method of accomplishing this, and in consequence many different methods are in use at the present day.

The different methods of pyloric exclusion can be divided into five groups:

1. Unilateral pyloric exclusion (Eiselsberg).
2. Submucous plastic (Girard).
3. Infolding method (Kelling-Mayo).
4. Exclusion method with the aid of autoplastic material (Wilms).

[1] From the Department for Surgical Research, College of Physicians and Surgeons, Columbia University, and the Surgical Service of the Montefiore Home, New York City.

5. Exclusion methods with the aid of foreign material (suture, etc.) (Kelling-Berg-Cackovic, Parlavecchio, Biondi).

The unilateral pyloric exclusion (Fig. 1*A*) has quite a unique position among all these different methods. For it is universally conceded, that Eiselsberg's method provides for a permanent occlusion of the pylorus. An exceptional case, as the most interesting case of Gerster, reported by Moschcowitz, does not depreciate the value of this method. However, all the other methods of excluding the pylorus, though heralded by their originators as permanent occlusion methods, have not been able to stand the experimental and clinical tests of other investigators, in so far as the question of permanent occlusion of the pylorus is concerned. Yet Eiselsberg's method is used and justly, only by a comparatively small number of surgeons. For this method is a much more formidable surgical procedure than any of the other methods. And though its absolute ultimate success must be granted, the comparatively great operative risk stands in the way of its general use for the treatment of pyloric and duodenal ulcer.

Girard's method is a reverse Heinecke-Mickulicz pyloroplasty applied to the seromuscularis, but leaving the mucosa intact. A transverse incision is made on the anterior surface of the prepyloric part of the stomach and the walls of the incision united in the longitudinal direction, thus producing a fold of the mucosa, which obstructs the lumen of the pylorus. This method does not seem to have gained popularity, probably because the stitch and band methods obtain the same object in a much more simple way.

The infolding stitch method (Kelling-Mayo) is shown in Fig. 1*B*, and the very simple technique does not require any further explanation. Tappeiner, who tested the different methods of pyloric exclusion in a series of animal experiments, showed that this method does not yield any permanent results. Furthermore, Moschcowitz and Wilensky have lately reported a case, in which they had occasion to test the permeability of the pylorus two weeks after the performance of a gastro-enterostomy, combined with the Mayo exclusion. The patient had to be re-operated upon because of intestinal obstruction. The post-mortem examination showed the pylorus to be patent, "no complete closure of the lumen of the pylorus had been obtained."

Wilms' method of pyloric exclusion (Fig. 1*C*) makes use of a free transplant of fascia (usually taken from the fascia lata) which is used as a constricting band around the pylorus. Kolb, an assistant of Wilms, has reported that this method has stood the test of animal experiments and clinical experience, especially in reference to the permanency of the exclusion. Baggio, however, found that the transplanted fascia was macroscopically and microscopically partly absorbed and necrotic, and the result by no means ideal.

I wish to discuss more in detail the last group, i.e., exclusion with the aid of sutures, wires, cotton tape, etc., because the experimental work, which I am going to describe in this paper, falls under this heading. Three different methods belong to this group: Kelling-Berg-Cackovic, Parlavecchio, Biondi. Though the methods fall in one group in that foreign material is used in all of them for the constriction of the pylorus, the technique differs widely.

Exclusion of the pylorus with the aid of a ligature (Fig. 1*D*) is not a new procedure. It was used by Kelling in animal surgery in 1899, and introduced into clinical surgery simultaneously and independently by Berg and Cackovic in 1903. A double Pagenstecher linen suture, armed with a needle, is carried around the posterior stomach-wall, and is held in place by taking several bites in the anterior wall of the stomach. The suture is then tied and the pylorus thus occluded; the knot is buried by a few single stitches (Berg). This exclusion stitch has acquired great popularity in the treatment of acute and chronic ulcers of the pylorus and duodenum.

Parlavecchio's method cannot be considered as a new one, but simply represents a slight modification of the method just described, in that he substituted a cotton tape for the Pagenstecher stitch. Randisi and Dominici have published excellent results with this method. Leriche, however, has reported that his results with this method were by no means satisfactory.

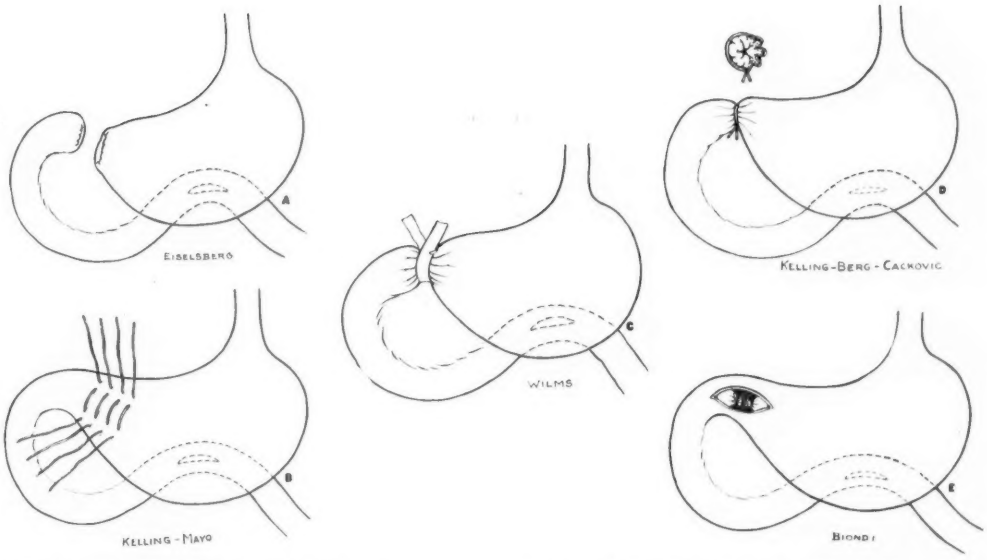

Fig. 1*A*. Von Eiselsberg method of pyloric exclusion.
Fig. 1*B*. Kelling-Mayo method of pyloric exclusion.
Fig. 1*C*. Wilms method of pyloric exclusion.
Fig. 1*D*. Kelling-Berg-Cackovic method of pyloric exclusion.
Fig. 1*E*. Biondi method of pyloric exclusion.

Biondi's method (Fig. 1*E*) was described in detail by Porta. A longitudinal incision is made across the pylorus through the serosa and muscularis, and the musculoserosa coat peeled away from the mucosa. The mucosa is then cut between two ligatures which have been tied around the tube of the mucosa at both ends of the incision. The stumps are carbolized and the seromuscularis incision closed with a few sutures.

The Biondi method undoubtedly stands midway between the very simple constriction methods (Mayo, Wilms, Berg, Cackovic) and Eiselsberg's unilateral exclusion. A perusal of the literature shows that none of the simple constriction methods assures permanent results. Eiselsberg's method, as already mentioned, is too great a surgical procedure. Biondi's method would meet all requirements, if the technique were as easy of performance as the constriction methods and as certain of permanency as the method of Eiselsberg.

It is obvious though that the method as described by Biondi can not assure a permanent closure of the pylorus. The ligature around the mucosa stumps is apt to cut through at an early date. Furthermore, the regenerative power of the mucous membrane is so forceful, that the small defect caused by the operation will heal over in a very short time, thus restoring the original state of affairs.

A permanent occlusion, however, would be assured, if instead of closing the linear incision in the seromuscularis, the stomach were to be divided and the two stumps buried in the pyloric and duodenal end respectively.

This modified method of Biondi is performed in the following manner: Gastroenterostomy. The gastrohepatic ligament is ligated in the pyloric region, which enables us to deliver the pylorus in front of the abdominal wall. The transverse incision through the seromuscularis (Fig. 2) is then carried around the pylorus. The muscularis is peeled away from the mucosa which is thus exposed intact for about one inch. The mucosal tube is ligated above and below (Fig. 3) with a silk or Pagenstecher ligature, cut in between the ligatures (Fig. 4), and the stumps carbolized. Figure 5 shows the burying of the stumps on the stomach end and on the duodenal end.

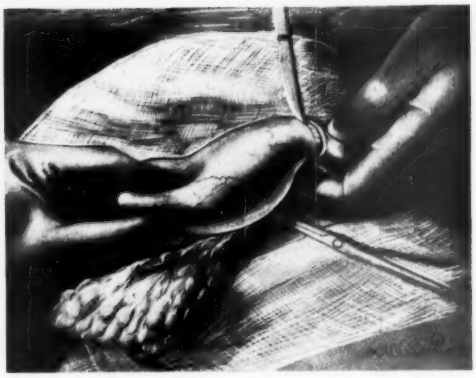

Fig. 2. Modified Biondi method showing incision of serosa and muscularis.

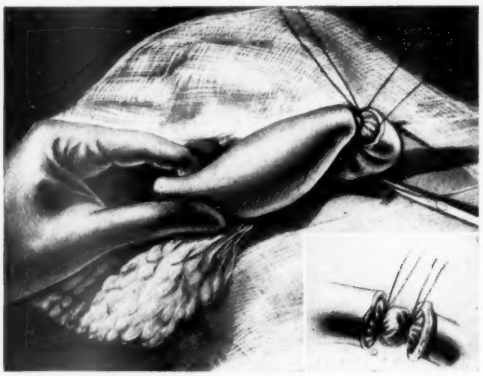

Fig. 3. Modified Biondi method showing ligation of mucous membrane.

The experimental work was done along two lines: (1) Exclusion of the pylorus according to Biondi, and (2) operations with the modified method, just described.

1. *Exclusion of the pylorus (Biondi).* This method was applied on five dogs. One dog, which showed some signs of distemper on the day of operation, died the next day. The other four dogs were observed a sufficiently long time to make the post-mortem findings of value. The results are the following: The occlusion was in place after fourteen days, (dog 256). After twenty-one and thirty-four days (dogs 320 and 96) the lumen had become re-established and admitted a medium-sized glass rod. The findings after eighty-seven days are shown in Fig. 6 (frontispiece). The only trace of any operative interference is one Pagenstecher stitch attached to the mucosa and protruding into the lumen of the stomach; otherwise the field of the operation in the pyloric region appears to be perfectly normal.

Microscopical examination (Fig. 7) (Pathological Accession No. 3,531): This section shows a portion of the pyloric end of the stomach and adjacent part of the duodenum. The mucous membrane is intact throughout (except for some artefacts in the section) and appears normal. The muscularis mucosæ is intact too throughout the length of the specimen. The submucosa appears somewhat thicker than normal and is composed of very dense fibrous tissue. Except for the thickening of the submucosa the section resembles a normal section of this portion of the gastro-intestinal tract.

2. *Exclusion of the pylorus (modified Biondi).* This series comprises five cases. In one case (dog 116) the result was spoiled by an error in technique. In peeling away the muscularis from the mucosa the latter was accidentally opened at the duodenal side and the intestinal contents escaped. The dog died the following day and the post-mortem examination showed a leakage of the duodenal stump. Another dog (29) died four days after the operation from an unknown cause. The operative result was perfect. Three dogs (103, 244, 155) were observed thirty-eight, sixty, and one hundred and fifty-four days respectively. In all of them the exclusion was perfect. This modification insures a permanent and absolute occlusion of the pylorus.

The advantages of the original Biondi method and its modification, as compared with the Eiselsberg method are the following: No extensive ligation is required. No clamps which take up a great deal of space are needed. The Biondi method does not form large stumps and therefore makes the infolding of these stumps much easier than does Eiselsberg's method.

The Biondi method would therefore be preferable to the Eiselsberg method, if the technique were an absolutely safe one. The technique, however, is by no means as simple, as Porta has claimed. The dissection of the muscularis from the mucosa is not as easy as appears from his description. My records show that during this process the mucosa was accidentally injured a few times. The great risk of this accident is obvious. As no clamps are applied in the Biondi method, leakage of intestinal contents and infection of the peritoneum are grave dangers of this procedure. Gibson and Beekman have already drawn attention to this difficulty in Biondi's technique. For the same reason, Strauss' method, a combination of the method of Wilms and

Fig. 4. Modified Biondi method showing division of mucous membrane.

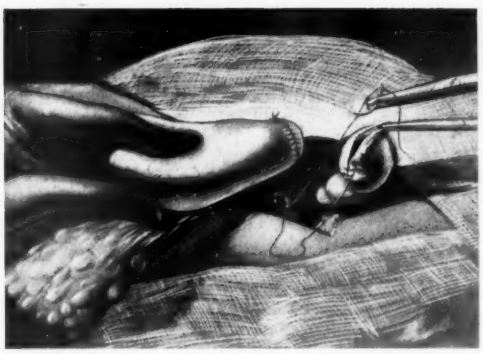

Fig. 5. Modified Biondi method showing the burying of the stumps.

Biondi, cannot be considered absolutely safe, though the results of his animal experiments are certainly very satisfactory.

This technical difficulty, however, would not prejudice us against this method, if it were really to assure a permanent occlusion of the pylorus. The specimen represented in Fig. 6 (frontispiece) shows conclusively, however, that the original Biondi method does not guarantee a permanent occlusion. It is really remarkable to observe the regenerative power of the gastro-intestinal mucosa of this specimen. Ligation of the mucous membrane in two places, division of the same between these ligatures, and carbolization of the stumps did not leave after two months a trace of any surgical interference, except one stitch still *in situ*.

If the Biondi method, as shown from our experiments, does not safeguard against reopening of the pylorus, we certainly cannot expect any permanent occlusion from the infolding and constriction methods (Mayo, Kelling, Berg, Wilms, etc.). We must agree with Leriche, who came to the conclusion that with the exception of Eiselsberg's method all the different forms of pyloric exclusion are "un parodie du l'exclusion vraie." It is perfectly true that none of these methods guarantee a permanent occlusion of the pylorus.

As far as the permanent result is concerned we cannot therefore agree with the statement of Berg that his method "effectually and permanently excludes the antral end of the stomach and duodenum from the passage of stomach contents through them."

That this statement is correct is proved by a human pylorus which I had occasion to resect a few months ago. The rarity of this specimen induces me to give the history somewhat in detail.

B. C., aged 24 years, was operated on by Dr. A. A. Berg, at the Beth David Hospital, for duodenal ulcer, in September, 1913. A gastro-enterostomy was made and the pylorus was occluded by an encircling stitch. The patient was relieved from her symptoms for a few months only. Afterward her symptoms reappeared and she entered the Montefiore Home. An exploratory laparotomy was performed by Dr. Charles Goodman, May, 1914. He found the gastro-enterostomy wide open and the pylorus patent. The upper part of the small intestines was studded with small grayish nodules. Diagnosis; Tuberculous peritonitis. After the second operation she was relieved of her symptoms for a while and then her old symptoms recurred. Radiography showed retention of food in the pyloric pouch, distal to the gastro-enterostomy. Though the possibility of a gastric neurosis (hysteria) was considered, it was deemed possible that a resection of the stomach near the gastro-enterostomy might relieve her symptoms.

Operation, July, 1915 (Lewisohn): Gas and ether anæsthesia: right pararectal incision; gastro-enterostomy is patent. The large intestine is of normal appearance, not dilated, no nodules on its surface. The small intestine is of normal caliber. The walls are soft, no ulcers are felt. On the surface of the proximal part of the ileum a few whitish nodules are noticeable. The pylorus is patent, admitting the little finger (Fig. 9). No ulcers are palpable at the pylorus or in the duodenum. On the anterior surface of the pylorus the old Pagenstecher stitch, situated

Fig. 7. Microscopical section of pyloric region 87 da after Biondi operation, Dog 246, No. 3,531. Path. Surg. (×30).

subperitoneally, is still in evidence. Resection of the pylorus and layer suture of both ends.

The patient was again free from vomiting for a while. Her symptoms, however, reappeared. Evidently she is suffering from a neurosis.

The specimen of the pylorus shows the stitch on the anterior surface, slightly curved; the knot is distinctly visible and intact. The mucous membrane does not seem to be atrophic on microscopical appearance. No remains of the stitch are noticeable on the posterior surface of the pylorus.

Microscopical examination of section from the anterior wall (Accession No. 3664) (Figs. 10 and 11): The wall of the pylorus (Fig. 10) appears considerably thickened at the constricted portion. The mucous membrane appears normal except for slight thinning of the constricted portion. The submucosa is much thickened, composed of dense connective tissue. The remains of the suture can be seen surrounded by an area of thickened connective tissue, round cells and giant cells. The muscularis is thickened at the point of constriction, the thickening being due to the increase in the connective tissue. Figure 11 shows very well finer details of the fate of the threads, distinctly surrounded by a ring of connective tissue; a great mass of inflammatory tissue and numerous giant cells are distinctly seen in this section. A bridge of connective tissue has

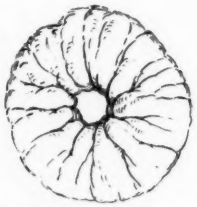

Fig. 9. View of pyloric lumen 20 months after pyloric exclusion (patient B. C.).

grown between the two parts of the double thread, separating them entirely.

Microscopical examination of section from the posterior wall (Accession No. 3690) (Figs. 12 and 13): A section from the posterior wall (Fig. 12) shows the same thickening of the submucosa, but in a much less marked degree. At the point of constriction the serous coat is very much thickened by an increased amount of fibrous tissue, in which the remains of the suture are visible. The muscularis is interrupted at this point by a narrow band of fibrous tissue, which runs from the submucosa to the serous coat. The mucous membrane appears entirely normal. Figure 13 shows finer details of the stitch and surrounding tissues. The findings are about the same as in Fig. 11. The mass of inflammatory tissue is larger than in the corresponding ection from the anterior wall. The giant cells are not quite as numerous.

This specimen shows conclusively that the occlusion was not a permanent one. This is in accordance with radiographic findings reported from different clinics. Radiographs taken a year or more after the exclusion show a re-opening of the pylorus in a great majority of cases. Pictures taken a few months after the exclusion are of no value; for it can be well conceded, that all these methods provide for a temporary exclusion of the pylorus. The re-establishment of the pyloric lumen following occlusion may be explained by the following hypothesis:

The constricting stitch, placed to occlude the pylorus, by its pressure gradually cuts through a part or the whole of the peritoneum, similarly through muscularis, through submucosa and mucosa. This process continues until the stitch has cut to the point where pressure is no longer exerted upon the tissues. Repair of the divided structure proceeds immediately behind the ligature, as it advances through the tissues. Thus at no time is there an opening in the intestinal wall. When the

Fig. 10. Microscopical section of anterior wall of pylorus (patient B. C., Surg. Path. No. 3,664). *a* Exclusion stitch. (×30).

Fig. 11. Same as Fig. 10. Threads surrounded by a dense ring of connective tissue, round and giant cells. (×200).

ligature comes to rest it is sometimes free in the pyloric lumen, sometimes it is embedded in the wall of the pylorus, as any non-absorbable suture material may be. The actual cutting process caused by the stitch takes place through degeneration, death and disintegration of the cells. The local compression of the vessels and cells deprives the tissue of nutrition, causing cell degeneration and death. Autolytic ferments and phagocytic activity lead to the cell disintegration and removal. The connective-tissue stroma, as the tissues come together behind the suture, proliferates, repairing the defect from the loss of cells. Cicatricial tissue therefore repairs and leads to regeneration of the intestinal wall.

I think that the arguments about the permanent anatomical exclusion of the pylorus and about the preference of one method over the other are rather futile. We can grant that with the exception of Eiselsberg's method or the modified Biondi method above described, none of the exclusion methods will insure a permanent occlusion. The argument is really academic only. The patient consents to an operation, because he wants to be relieved of his symptoms. It is immaterial to him, whether his pylorus is patent after a certain time, as long as he is permanently cured.

It is evident that all we have to do to obtain that result is to prevent food and stomach juice from coming in contact with the ulcer for a few months (or possibly for a few weeks only). A temporary absolute exclusion of the pylorus, not a permanent one, is needed. This purpose is just as well obtained by the exclusion stitch with a Pagenstecher suture, which seems to be technically the most simple procedure, as by any of the other more complicated methods (Wilms, Biondi, etc.).

CONCLUSIONS

1. With the exception of Eiselsberg's unilateral exclusion and the modified Biondi method, none of the different methods of

Fig. 12. Microscopical section (Surg. Path. No. 3,690) of posterior wall of pylorus (patient B. C.). *a* Exclusion stitch. (×30).

exclusion guarantees a permanent, occlusion of the pylorus.

2. An absolute, though temporary exclusion of the pylorus provides for a permanent cure of pyloric and duodenal ulcers.

3. The most simple method from a technical standpoint is the exclusion stitch (Kelling-Berg-Cackovic). This stitch should be used in preference to the more complicated methods (Wilms, Parlavecchio, Biondi).

4. The Eiselsberg's method and the modification of the Biondi method, though guaranteeing a permanent exclusion, are technically too complicated and should not be used.

5. The clinical results are just as good in using the most simple method (exclusion stitch) as in the use of the most complicated method (Eiselsberg). The exclusion stitch is therefore the method of choice for the treatment of pyloric and duodenal ulcers.

Records of Animal Experiments

A. Biondi method

Dog 348. Previous gastro-enterostomy had been done by students, May 3, 1915. Dog has some distemper. *Operation*, May 11, 1915: Pararectal incision, pylorus brought forward, pyloric artery tied; seromuscular coat incised and liberated from mucosa; mucosa ligated above and below (silk) and cut in between; stump carbolized and buried; layer suture of abdomen. May 12: Dog died of distemper. *Post-mortem examination:* No peritonitis; gastro-enterostomy patent. Exclusion stitches in place. *Observation time*, one day.

Dog 256, Surg. Path. No. 3,407. *Operation*, March 23, 1915: Gastro-enterostomy posterior antecolica; gastrohepatic ligament ligated and cut, thus facilitating protrusion of pylorus in front of abdominal wall; pylorus cut, mucous membrane ligated in typical fashion; central ligature, cut by mistake, reapplied; seromuscularis sutured; layer suture of abdomen. April 6: Killed on account of distemper. *Post-mortem examination:* Peritoneum smooth; gastro-enterostomy functionating; exclusion evidently holding. *Observation time*, fourteen days.

Dog 320, Surg. Path. No. 3,485. *Operation*, April 27, 1915: Median laparotomy; suture gastro-enterostomy; longitudinal incision of seromuscularis over pyloric region; mucosa freed all around and cut through between two ligatures; stumps covered by musculoserosa suture; abdomen closed. May 17: Died of bronchopneumonia. *Post-mortem examination:* Gastro-enterostomy patent. Pylorus is patent again for medium-sized glass rod. *Observation time*, twenty-one days.

Dog 96, Surg. Path. No. 3,251. *Operation*, November 24, 1915: Typical gastro-enterostomy posterior antecolica; exclusion of pylorus; small longitudinal incision over pyloric region through serosa and muscularis; attempt to strip muscularis from mucosa very difficult as tissues are adherent to one another; therefore, transverse incision added, encircling most of the stomach. December 28: Died of lobar pneumonia. *Post-mortem examination:* No peritonitis. Specimen removed *in toto*. Pylorus patent. *Observation time*, thirty-four days.

Dog 246, Surg. Path. No. 3,531. *Operation*, March 17, 1915: Gastro-enterostomy posterior antecolica; typical pyloric exclusion according to Biondi. Exclusion technique worked very well in this case. Stumps covered with seromuscularis coat. June 8: Killed. *Post-mortem examination:* Removal of stomach, duodenum, and upper part of jejunum. Gastro-enterostomy patent. No outside scar visible in pyloric region. Omentum slightly adherent to this region. The pylorus is perfectly open, exactly like a normal pylorus. Stomach opened along the lesser curvature, into the duodenum. The pyloric-duodenal junction is perfectly normal. One Pagenstecher stitch lying in this region is the only sign of operative interference (Fig. 6 frontispiece). *Observation time*, eighty-seven days.

B. modified biondi method

Dog 116. *Operation*, December 8, 1914: Gastro-enterostomy posterior antecolica with clamp; pylorus cut on its anterior surface through serosa

and muscularis, after freeing the pylorus from its attachment (gastrohepatic ligament). In trying to pass an aneurism needle around the mucous membrane, the latter was pierced and some stomach contents escaped. Suture of both duodenal and stomach end of the mucosa, inverting suture of both stumps, which is very unsatisfactory on the duodenal end; closure of abdominal wall. December 9: Died of peritonitis. *Post-mortem examination:* Peritonitis in upper abdomen; leakage of duodenal stump. Stomach end of resection in good condition and gastro-enterostomy perfect. *Observation time*, one day.

Dog 129. *Operation*, December 15, 1914: Typical gastrojejunostomy; pylorus freed all around and brought outside of abdominal parietes; transverse section through serosa and muscularis in anterior and posterior aspect of stomach; ligature of mucous membrane above and below (Biondi), and inversion of stumps of stomach and duodenal end, closure of abdominal wall in layer sutures. December 19: Died. *Post-mortem examination:* No peritonitis; exclusion in good condition; specimen lost in transit. *Observation time*, four days.

Dog 103, Surg. Path. No. 3,261. *Operation*, December 1, 1914: Typical gastro-enterostomy posterior antecolica; a cross incision made over the pylorus on the anterior wall of the stomach, and serosa muscularis peeled back from mucosa; an aneurism needle was carried around the mucous membrane at the posterior wall and the mucous membrane ligated between two silk ligatures and cut in between; the stumps were carbolized; the rest of the seromuscularis coat was now divided and a running suture united the incision at the stomach end, thus burying the mucous membrane stump. Same procedure for duodenal end. Suture of abdominal wall. January 7, 1915: Dog died. *Post-mortem examination:* Bronchopneumonia. Peritoneal cavity normal. Exclusion perfect. No local peritonitis around excluded part. Right middle lobe of lung shows extensive pneumonia. *Observation time*, thirty-eight days.

Dog 244, Surg. Path. No. 3,544. *Operation*, March 16, 1915: Gastro-enterostomy posterior antecolica; longitudinal incision one inch long across pylorus, cutting through serosa and muscularis; the stripping off of the muscularis from the mucosa successful only after small transverse incision had been added; pin-hole opening accidentally made in mucosa; double silk ligature then carried around on aneurism needle, tied proximally and distally and mucosa cut through in between; stumps carbolized; musculoserosa incision sutured over stumps. June 15: Killed. *Post-mortem examination:* Gastro-enterostomy patent. Pyloric exclusion perfect at both ends (stomach and duodenum). *Observation time*, sixty days.

Dog 155, Surg. Path. No. 3,543. January 12, 1915: Typical posterior gastro-enterostomy. Pylorus then cut across transversely after ligating gastrohepatic ligament. Cut down to mucosa.

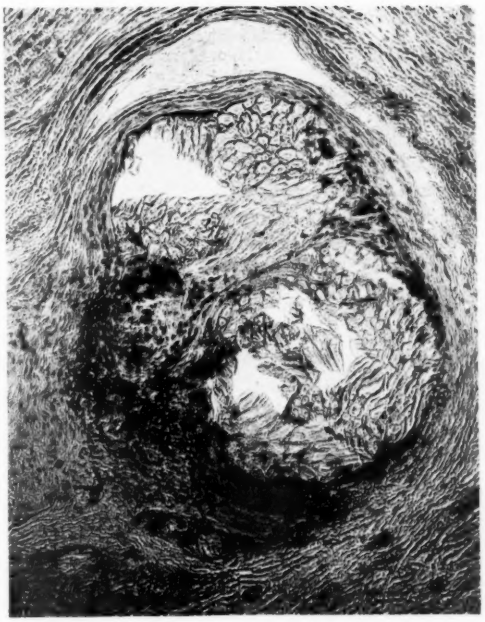

Fig. 13. Same as Fig. 12. Same findings as in Fig. 11. The defects in the cross section of the linen threads are artefacts, caused by the microtome knife. (×200).

Muscularis stripped away from mucosa with some difficulty. Ligatures tied around mucosa sac above and below and cut in between. As both ligatures were too near each other, they slipped off. Openings closed with suture and then buried. Layer suture of abdomen. June 15: Killed. *Post-mortem examination:* Gastro-enterostomy patent. Inner silk suture still in place on one spot. Occlusion of pyloric end of stomach and duodenum perfect. *Observation time*, one hundred and fifty-four days.

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THE END-RESULTS OF FOURTEEN OPERATIONS FOR PERFORATED GASTRIC AND DUODENAL ULCERS[1]

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THE series of cases here reported were operated on by me or my associates, Doctors Hitzrot and Lee, at the New York Hospital, since February 11, 1913, a little less than three years. This series does not include any cases previously reported by me in other publications. All patients surviving (13) have been carefully followed as regards their after-history and end-results. In 10 cases we have gastric analyses and in 12 cases X-ray pictures of the stomach. The summary of their condition is shown in Table I. All the patients were males, the average age 35. The average duration of the perforation before operation was about ten hours, and to this relatively short period of time must be attributed the main factor in obtaining the 92 per cent of successful cases. The perforation was situated in the duodenum in 7 cases; in the stomach, but close to the pylorus, in 7 cases. Case 12 had two simultaneous perforations of the duodenum. Only three cases gave a history of freedom from previous or obvious gastric disturbances (Cases 1, 9, and 13); the others giving characteristic histories of ulcer trouble, some going back as far as fifteen years. Case 8, the fatal case, was obviously hopeless and probably an operation would not have been attempted by most surgeons. It has been our policy always to give every case, no matter how desperate, a possible chance of recovery, which sometimes occurs. The symptoms dated back thirty-six hours; there was a recognizable general peritonitis and operation was performed only after a saline infusion, the patient surviving only two hours.

We have been impressed with Deaver's statement that the patient improves in these cases after the peritoneum has been opened, allowing the escape of free intestinal gas. In a few cases blood-pressures have been taken throughout the operation to determine whether this improvement is borne out by the rise in blood-pressure. Our findings, however, are contradictory and inconclusive.

FREQUENCY AS COMPARED TO OTHER ACUTE ABDOMINAL CONDITIONS

Collinson[2] says, "Perforation of a gastric or duodenal ulcer is with the exception of appendicitis the most frequent acute abdominal lesion." Our experience does not verify

[2] J. Am. M. Ass., 1914, October 3.

[1] Read before the Chicago Surgical Society, January 7, 1916. (See discussion, p. 498.

TABLE I—ACUTE PERFORATIONS OF STOMACH AND DUODENUM

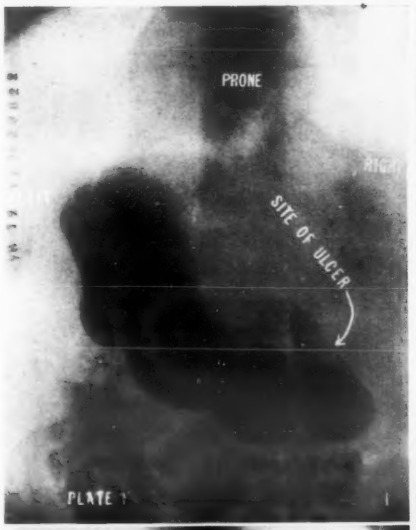
No. of Case	Age	Diagnosis	History of Perforation	Time Between Admission to Hospital and Operation	Soft Solid Diet After Operation	Allowed up After Operation	Discharged After Operation	Gain in Weight After Operation	X-ray Findings After Operation	Gastric Analyses
1	26	Duodenal ulcer	2½ hours	1 hour	3 days	15 days	21 days	2¼ pounds in 1 month	Slight gastric retention — 1 month	Well marked hyperacidity. (1 mo. after operation.)
2	32	Gastric ulcer	24 hours	50 minutes	7 days	21 days	23 days	Regained normal weight in 1½ years	No gastric retention — 1½ years	Acidity approximately normal. (1½ yrs. after operation.)
3	51	Gastric ulcer	8 hours	45 minutes	4 days	24 days	34 days	47 pounds in 8 months	Moderate gastric retention — 1 year 8 months.	Acidity less than normal. (1 yr. 8 mos. after operation.)
4	47	Duodenal ulcer	3 hours	2½ hours	7 days	12 days	13 days	20 pounds in 9 months	No data	No data.
5	37	Gastric ulcer	2¼ hours	50 minutes	7 days	11 days	15 days	22 pounds in 1 year	No gastric retention — 1 year	No data.
6	38	Gastric ulcer	18 hours	5¼ hours	5 days	22 days	24 days	Gaining in weight after 1 year	No gastric retention — 1 year	Hyperacidity.
7	43	Duodenal ulcer	3 hours	50 minutes	4 days	26 days	30 days	13 pounds in 2 months	Slight gastric retention — 2 months	Well marked hyperacidity. (2 mos. after operation.)
8	34	Gastric ulcer	36 hours	45 minutes	*					
9	26	Duodenal ulcer	3 hours	2 hours	10 days	14 days	18 days	Normal weight in 1 yr. 9 mos.	No gastric retention — 1 year 9 months	Acidity approximately normal. (1 yr. 9 mos. after operation.)
10	28	Duodenal ulcer**	5 hours	4¾ hours	11 days	13 days	16 days	No data	Slight gastric retention — 4 months.	No data.
11	57	Duodenal ulcer	7 hours	1 hour	8 days	11 days	15 days	Gained in weight in 2 months	No gastric retention — 2 months	Test-meal passed before it could be expressed.
12	27	Duodenal ulcer (double)	3½ hours	1¾ hours	4 days	10 days	11 days	20 pounds in 2 yrs. 10 mos.	No gastric retention — 2 yrs. 10 months.	Acidity less than normal. (2 yrs. 10 mos. after operation.)
13	23	Gastric ulcer	2 hours	45 minutes	5 days	15 days	18 days	12 pounds in 2 months.	No gastric retention — 2 months	Test-meal passed before it could be expressed.
14	21	Gastric ulcer	2½ hours	1¼ hours	5 days	12 days	14 days	7 pounds in 3 months	Considerable gastric retention and ptosis of stomach — 3 mos.	Acidity less than normal. (3 mos. after operation.)

* Case considered hopeless before operation. Saline infusion. Patient died two hours after operation. (Acute general peritonitis.)
** Only case in which gastro-enterostomy was performed.

this statement, as in the same period of time we have had occasion to operate on 35 cases of acute intestinal obstruction.

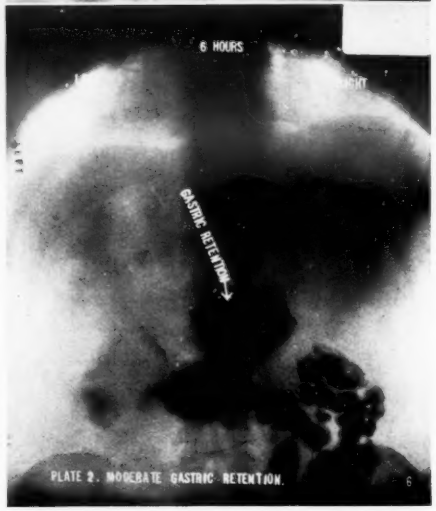
DIAGNOSIS

When seen early, the diagnosis of a perforation presents little difficulty. The frequent history of previous gastric disturbance, the violent onset with sharp stabbing pain, more or less collapse, the boardlike rigidity of the abdominal muscles, particularly of the upper abdomen, the possible vomiting of blood, are absolute characteristics. An additional but fleeting symptom I have observed in a few cases is a sharp pain coming usually within the first hour after perforation and referred to either supraclavicular fossa, chiefly the left, which lasts usually only a few minutes and disappears entirely. When the patient comes under observation later and in the absence of satisfactory history, while we can readily make a diagnosis of peritonitis the exact origin is not so clear, particularly with the tendency of the extravasated material to gravitate toward the right flank and simulate a spreading peritonitis from a perforated appendix. In fact a considerable proportion of the cases of perforated gastric ulcer in the



Figs. 1 and 2. Case 1, roentgenograms taken one month after operation.

Figs. 3 and 4. Case 2, roentgenograms taken one and a half years after operation.



Figs. 5 and 6. Case 3, roentgenograms taken 8 months after operation.

later stages are operated on, and perhaps always will be, for an appendix. The diagnosis, however, to the experienced operator is clearly obvious from the escape of gas, sour smell as opposed to colon bacilli smell, and the mucilaginous character of the fluid. Even if the incision is placed over the appendix, if the possibility of a perforated ulcer has been considered, one can increase the likelihood of recognition of this condition by opening the peritoneum under water, a procedure which I have used for a number of years.

The value of obliteration of the liver dulness as a diagnostic sign. This symptom I have never been able to recognize in any perforation of any kind of the gastro-intestinal tract, and I feel it is a great pity that it is allowed to remain as one of the possibilities of diagnosis.

OPERATIVE METHODS

A description of these will comprise consideration of the following:

1. Anæsthesia.
2. Site of incision.
3. Method of dealing with perforation.
4. Performance or not of a gastro-enterostomy.
5. Cleansing of abdomen.
6. Drainage.

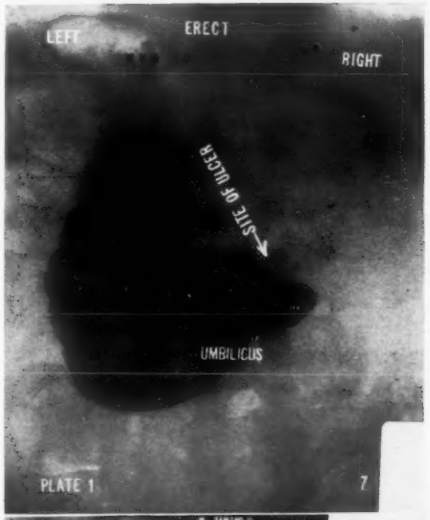
In outlining an operative program our ideal should be to perform a simple, easy, and quick operation which will jeopardize the patient's strength as little as possible, deal efficiently and safely with the present condition and, if feasible, forestall the continuance or occurrence of a gastric lesion.

1. A general anæsthetic, preferably ether, is necessary. It may wisely be preceded by a generous hypodermic of morphine.

2. The great majority of perforations lie to one side or the other of the pyloric vein, proximal gastric, distant duodenal ulcer. An incision through the middle or outer border of the upper part of the right rectus muscle gives the most direct approach to the pylorus. It should be made quite large so as to allow for easy and quick recognition and access to the lesion. The several layers are incised down to the peritoneum. At this stage the edges of the muscular incision on either side are seized and held up by the assistant, thus forming a crater, the bottom of which is the as yet unopened peritoneum. Two fine Kocher clamps seize the peritoneum, the crater is filled with fluid, the knife nicks between the two clamps, and any gas in the peritoneal cavity is obvious, coming out as bubbles through the layer of water. Ordinarily the presence of gas is sufficiently obvious, but with a very minute perforation and a very small amount of air this procedure will give a certainty, and of course it is of great advantage to get this definite information as we know that we must absolutely find a perforation whose existence is demonstrated by this test. Knowing where the lesion should be, we at once expose the pylorus when the perforation, situated anteriorly, becomes easily recognizable. The average perforation is at the center of an indurated area and is of such a size as to be clearly recognizable. Some of these perforations may not exceed the caliber of a steel knitting needle. If there is any difficulty in locating the perforation, pressing the gas from the stomach usually makes it obvious. In difficult cases insufflation of the stomach will help.

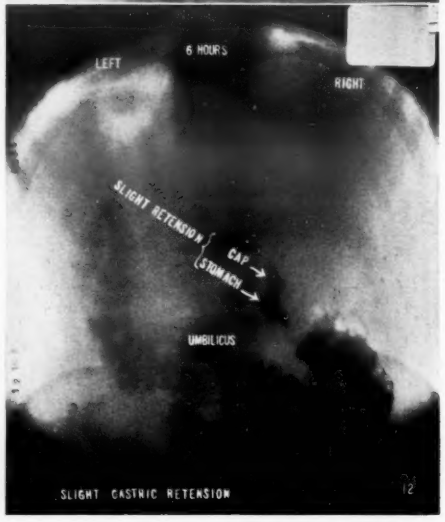
3. It is only exceptionally that anything more than a double purse-string suture of catgut is required to close the perforation. In order to get away from the friable indurated edges it may be necessary to make this purse-string rather wide. If possible it should be applied across the diameter of the viscus rather than lengthways for fear of narrowing the outlet. I believe that actual stenosis of the pylorus very seldom follows, even in cases where apparent kinking from the suture seems to result.

Case 12 shows very well that an apparent obstruction, the result of suturing of the perforation, does not necessarily cause subsequent constriction. In this case two simultaneous perforations of the duodenum were separately sutured with a purse-string and some constriction was apparently produced. X-ray examination nearly three years after operation shows no gastric retention in the six-hour plate and the patient has gained twenty pounds. It is interesting to note also that the acidity of the gastric contents is less than normal.



Figs. 7 and 8. Case 5, roentgenograms taken one year after operation.

Figs. 9 and 10. Case 6, roentgenograms taken one year after operation.



Figs. 11 and 12. Case 7, roentgenograms taken 2 months after operation.

One must remember that this narrowing is not a circular constriction but applies only to one face of the viscus, and we know by experience the tendency of these slighter distortions to become smoothed out. I have no experience with the more complex methods of closure and have never seen an indication for excision of an ulcer. Theoretically, it might seem that excision of an ulcer was indicated, but my experience leads me to believe that ulcers treated as I have described above show little tendency to give rise to future trouble. I feel distinctly authorized to make this statement as the result of the study of the series of cases now under consideration. My chief reason for thinking that such ulcers do not give rise to further trouble, lies in the belief that the perforation of an ulcer is *per se* a curative process. The perforation means usually the separation of the necrotic tissue with a natural tendency to union of the healthy surfaces left after the elimination of the foreign material.

4. The performance or not of a gastro-enterostomy is perhaps the subject which is most actively under discussion in connection with acute perforations of the stomach and duodenum and there is still wide divergence as to the proper attitude. My belief is that there would not be so much discussion if more care had been given to studying the end-results of operations for these perforations. I found statements regarding the after-condition of patients to be rather vague, incomplete, and wholly unsatisfactory as regards definite information, and I found a total absence of any study such as I have made in this series of cases and from which I largely base my opinions. The indications, certainly theoretically, for performing gastro-enterostomy are (1) to remedy any possible obstruction of the pylorus resulting from the methods of closure or the subsequent cicatrization of the ulcer, and (2) to bring about the cure of the ulcer as the action of gastro-enterostomy in changing the chemistry of the stomach unquestionably is a curative measure for many ulcers and particularly those of the duodenum. I admit that gastro-enterostomy may rarely be indicated to forestall stenosis.

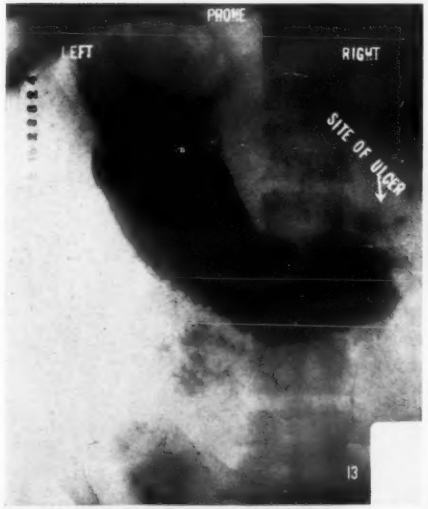
This series includes only one case of gastro-enterostomy performed with the belief that the repair had materially obstructed the gastric outlet, but as I have stated before the obstruction is probably more seeming than real and this view is borne out by the examinations which will be described later in detail.

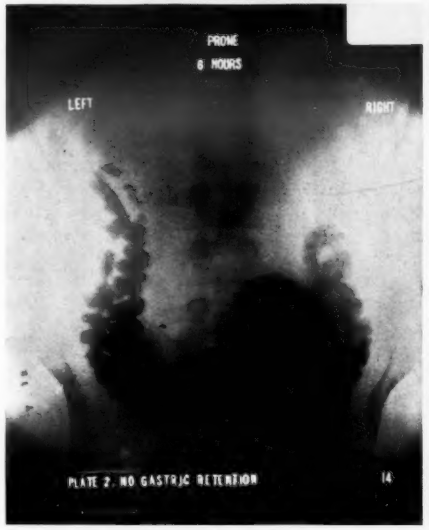
I reject gastro-enterostomy as a curative measure in this class of cases notwithstanding that I have had very gratifying experiences with it in the cure of chronic ulcer. I consider it unwise to do gastro-enterostomy for a condition which is going to be cured anyhow. In a very small number of cases in which gastro-enterostomy may possibly become necessary, it can be wisely postponed until its indications are clearly recognizable. The small number of cases in which it may become necessary will probably be balanced by the number of cases in which the gastro-enterostomy fails to prove satisfactory, either because it is improperly placed, too small (subsequent shrinkage), too large (a very disagreeable condition), or the rare but exceedingly grave gastrojejunal ulcer. Moreover, in dealing with acute perforations it seems wiser to do only what is absolutely necessary and not subject the patient, who may have to struggle with a possible peritonitis, to an unnecessarily long operation, or risk the spreading of the infection by the performance of a gastro-enterostomy under imperfect aseptic conditions. The after-history of this series of cases contains no instance in which we have occasion to regret the omission of this step.

In the mass of recent literature on the subject three very interesting communications have dealt particularly with this subject. Eliot [1] summarizes a painstaking investigation as follows:

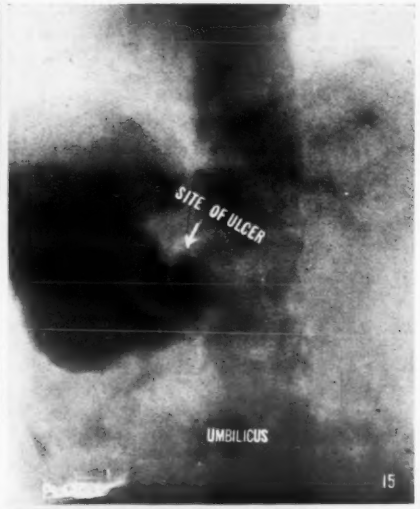
> That on the other hand, so many patients are evidently completely cured by the closure of the perforation, that they remain in good health for such a long time afterward and taking into consideration, moreover, the fact that, gastro-enterostomy for either benign stenosis or ulcer is no guarantee against future perforation or fatal hæmorrhage, the conclusion seems warranted that where an immediate gastro-enterostomy is not indicated by prior constriction of the pylorus or by constriction resulting from the necessary closure of the perforation, it is on the whole best to omit that operation until the future can decide whether the per-

[1] Am. J. Surg., 1908, October.





Figs. 13 and 14. Case 9, roentgenograms taken one year after operation.



Figs. 15 and 16. Case 10, roentgenograms taken 4 months after operation.

Figs. 17 and 18. Case 11, roentgenograms taken 2 months after operation.

sistence of the gastric symptoms or their recurrence will render it necessary or not.

Deaver [1] is a strong advocate of gastro-enterostomy. He says: "Infolding of a duodenal ulcer, if complete, is usually impossible without serious obstruction to the viscus. Therefore, gastro-enterostomy is essential." In six years he has had 25 operative cases with 1 death. I note, however, in that period of time that 6 of his patients died of this condition without any attempt at operation.

Collinson, in 1914, reported a series of 40 acute perforations of the duodenum with 13 deaths; 13 of the stomach with 7 deaths. He says: "An infolding of the pylorus or duodenum which at the time appears to provide a considerable grade of stenosis subsequently gives rise to no subsequent obstruction." In 14 cases which he treated by primary gastro-enterostomy 9 are quite well, 1 since died of carcinoma, and 1 had excision of a large gastrojejunal ulcer. He makes five points about the performance of gastro-enterostomy. His fifth is "Both to those who are experienced and those who are not I would make the following suggestion—when in doubt, don't."

It must be remembered also that gastro-enterostomy is no certain protection against the future development of ulcer or perforation.

Exclusion of the pylorus after gastro-enterostomy. If for any reason gastro-enterostomy had been done the question may well come up whether it may be wise to occlude the pylorus. Theoretically this procedure should more completely give the ulcer a chance to heal with physiological rest and give a better guarantee of the integrity of the suture. The whole question of the necessity, value, and efficiency of pyloric exclusion is still *sub judice*, and in my own mind I am far from clear as to its indications or the best means of performing it. I have not had occasion to apply it at any time in the treatment of a perforated ulcer, but I believe its possible advantages should be considered in the exceptional case, particularly one presenting an obstacle to the perfect closure of the perforation.

[1] Tr. Phila. Acad. Surg., 1914.

5. Cleansing of the abdomen. Depending on the duration and the size of the perforation, there will be a variable amount and nature of material. With very early intervention and a minute perforation there is only a little material immediately around the site of the perforation and this can be readily mopped up with pads. If there is a large amount of material, especially in the late stages, an attempt should be made to remove it so thoroughly as is feasible. In our operating room we have constantly available a suction apparatus, and by passing the tube to different parts of the abdomen fluid is readily evacuated. I am not in favor of washing out the material, lest the infection be spread.

6. Drainage. Many, perhaps most, operators rely on some form of drainage. I used to use it freely but have discarded it entirely of recent years during which my results have improved. The drainage may be *in situ*, tube or gauze led down to the site of intervention. It is possible that in a case of very unsatisfactory closure a prophylactic drainage tract might be established. Drainage of the pelvis by a separate stab wound is advised by many. Some operators also recommend the evacuation of the stomach with a tube after closure of the perforation.

AFTER-CARE

My own practice probably varies from that of many other operators, but I have had reason to feel satisfied with its results, as a great bulk of these patients operated on by simple, rapid method without gastro-enterostomy give a particularly speedy and comfortable convalescence. Two-thirds of the cases were out of bed in 15 days or less. In the first twenty-four hours the treatment is that usual to abdominal operations, nothing by mouth, semirecumbent position, Murphy drip. On the second day, water and other clear fluids in increasing amounts. By the fifth day the average case is allowed soft solids. At the time of discharge from the hospital all the patients were able to take and did take regular hospital diet. I insist particularly on this point because I think it is about time we got away from the fetish of underfeeding or of the particular value of

Figs. 19 and 20. Case 12, roentgenograms taken 2 years, 10 months after operation.

Figs. 21 and 22. Case 13, roentgenograms taken 2 months after operation.

Figs. 23 and 24. Case 14, roentgenograms taken 3 months after operation.

certain kinds of diets. It might be assumed that the subsequent success of these cases might be attributed to an "ulcer cure," but nothing of the sort was attempted and the cure can be ascribed only to the natural unhampered healing process.

AFTER-HISTORY

All 13 of our patients have remained under observation and we have accurate notes of their condition. In all the cases every patient on re-examination has shown an improvement in general health and relief or cure of previous gastric symptoms. The relief is most marked in the cases longest under observation. In several cases, notably Cases 3 and 4, the general restoration to health is most marked. Both these men were middle-aged, in poor general condition, and alcoholic. Their entire appearance and condition have improved to a degree that is most remarkable, amounting almost to rejuvenation.

The improvement of these patients' condition, particularly as regards freedom from gastric manifestations, is particularly striking if we contrast the previous history as given on admission and the detailed notes that we have kept from time to time as regards their condition.

CASE 1. *Previous history:* No history of gastric disturbance.

After-condition: One month post-operative, no pain. General diet. Gaining a little flesh. Feels pretty well. Ewald: Amount 40 ccm.; hydrochloric acid 70, total 80, combined 85, guaiac, none.

X-ray findings: Slight gastric retention. (Figs. 1 and 2.)

CASE 2. *Previous history:* History of stomach trouble for past 15 years.

After-condition: One and one-half years post-operative. No gastric symptoms. Normal weight. Eats everything. Ewald: Amount 100 ccm.; hydrochloric acid 50, total 65, combined 40, guaiac, none.

X-ray findings: No gastric retention. (Figs. 3 and 4.)

CASE 3. *Previous history:* History of gastric disturbance dating back four or five years. About two years ago had 14 hæmorrhages from the stomach in two weeks.

After-condition: One year 8 months post-operative. Condition exceedingly good. Has gained 47 pounds. Ewald: Amount 70 ccm.; hydrochloric acid 28, total 46, combined 32, guaiac, none.

X-ray findings: Moderate gastric retention. (Figs. 5 and 6.)

CASE 4. *Previous history:* Stomach trouble for past 15 years. No X-rays.

After-condition: Nine months post-operative. No gastric symptoms. Eats everything. Gained twenty pounds.

CASE 5. *Previous history:* "Chronic indigestion" for 10 years.

After-condition: One year post-operative. General condition greatly improved. No gastric symptoms. Has gained 22 pounds.

X-ray findings: No gastric retention. (Figs. 7 and 8.)

CASE 6. *Previous history:* Gastric disturbance for five or six years.

After-condition: One year post-operative. Since operation has been in excellent health. Only once recently sharp epigastric pain without relation to taking of food, but it has now disappeared. Ewald: Amount 25 ccm.; hydrochloric acid 60, total 80, combined 62, guaiac, none.

X-ray findings: No gastric retention. (Figs. 9 and 10.)

CASE 7. *Previous history:* Indigestion for past 5 years.

After-condition: Two months post-operative. Feels well. Eats everything. Has gained 13 pounds. Ewald: Amount 20 ccm.; hydrochloric acid 64, total 89, combined 30, guaiac, none.

X-ray findings: Slight gastric retention. (Figs. 11 and 12.)

CASE 8. *Previous history:* Indigestion for one year.

After-condition: Patient died two hours after operation. Had recognizable general peritonitis and operation was performed only after a saline infusion.

CASE 9. *Previous history:* No previous attacks. Patient had been troubled with a little indigestion but thought nothing of it.

After-condition: One year post-operative. Feels well. Occasional discomfort in epigastrium. Weight normal. Ewald: Amount 45 ccm.; hydrochloric acid 45, total 70, combined 60, guaiac, none.

X-ray findings: No gastric retention. (Figs. 13 and 14.)

CASE 10. *Previous history:* History of gastric disturbance dating back two years.

After-condition: Four months post-operative. No digestive symptoms. Splendid condition.

X-ray findings: Slight gastric retention. (Figs. 15 and 16.)

CASE 11. *Previous history:* Indefinite history of indigestion for past seven or eight months.

After-condition: Two months post-operative. No pain. Eats everything. Gaining in weight. Ewald meal passed before it could be expressed.

X-ray findings: No gastric retention. (Figs. 17 and 18.)

CASE 12. *Previous history:* Patient has been troubled with attacks of indigestion during past two years.

After-condition: Two years 10 months post-operative. Eats everything. Has gained 20 pounds.

Figs. 21 and 22. Case 13, roentgenograms taken 2 months after operation.

Figs. 23 and 24. Case 14, roentgenograms taken 3 months after operation.

Figs. 25 and 26. Case 15, roentgenograms taken 2 years, 10 months after operation.

Feels well. Ewald: Amount 40 ccm.; hydrochloric acid 0, total 10, combined 5, guaiac, none.

X-ray findings: No gastric retention. (Figs. 19 and 20.)

CASE 13. *Previous history:* No history of gastric disturbance.

After-condition: Two months post-operative. No pain. Eats everything. Has gained 12 pounds. Ewald passed before it could be expressed.

X-ray findings: No gastric retention. (Figs. 21 and 22.)

CASE 14. *Previous history:* Gastric disturbance dating back one month.

After-condition: Three months post-operative. General condition much improved. Gained 7 pounds. Eats anything. Occasional pain in epigastrium but no gas or vomiting. Ewald: Amount 30 ccm.; hydrochloric acid 48, total 95, guaiac, none; very few food particles.

X-ray findings: Considerable gastric retention. Ptosis of stomach. (Figs. 23 and 24.)

It has seemed necessary, however, to offer more definite evidence of the good condition of our patients than is contained in the above statement and in Table I. So far as is feasible with these hospital patients in a large city we have tried to have them return for gastric analyses and X-ray pictures of their stomachs. Most of these examinations are of very recent date, forming for the earlier cases a valuable end-result. Twelve of the cases have had bismuth pictures of the stomach, and the findings are shown in the accompanying photographs. Seven cases show no gastric retention at all. Two cases show only a negligible trace. Of the three other cases only one shows a considerable amount and the cause of this is quite likely to be a marked ptosis of the stomach. Case 10 shows a slight retention, notwithstanding a functionating gastro-enterostomy. In none of these cases is there any evidence, objective or presumptive, of any appreciable stenosis of the pylorus or duodenum.

Ten patients have had gastric analyses. In two cases the gastric analyses could not be carried out because the Ewald meal was passed so quickly. This evidence, however, is valuable as showing the total absence of obstruction to the gastric outlet. In three cases the gastric analyses show acidity to be approximately normal; in three cases there was well marked hyperacidity; in two cases the acidity was less than normal.

CONCLUSIONS

1. The most important feature in the consideration of acute perforating gastric and duodenal ulcers is a prompt recognition and operation. Patients operated on within a few hours, say two to four, should not have a mortality much in excess of 5 per cent.

2. As a routine, only the simplest, speediest but sufficiently efficient operative procedure should be employed.

3. Such operations as resection of the ulcer and gastro-enterostomy should be the exception and performed only under very distinct indications, chiefly to overcome definite stenosis produced by closure of the perforation. It must be remembered that many artificial stenoses are apparent rather than real. Operations, such as resection or gastro-enterostomy intended to bring about the cure of the ulcer, are really unnecessary, as a careful study of the cases treated by the ordinary measures shows a tendency to spontaneous cure of the ulcer as a result of the perforation. It might almost be said that the perforation is a blessing in disguise. To judge properly of the value of operative procedures all cases should be carefully followed with accurate records of the findings. Analyses made from such records dispel many of the loose and inaccurate views now held.

THE TROPHIC ELEMENT IN THE ORIGIN OF GASTRIC ULCER [1]

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IT has been found that gastric ulcer can easily be produced by the following conditions:

1. By lesions of the central nervous system.

2. By lesions of the gastroduodenal nerves; i.e., disturbing the innervation of (a) the vagus cervicalis, thoracic subdiaphragmatic, (b) the sympathetic nervous system in the rami which communicates between the fifth and ninth dorsal vertebræ in the thoracic and subdiaphragmatic splanchnic nerves, in the solar plexus, and in the lumbar chain.

3. Through local circulatory disturbances by means of embolism.

4. Through ligation of the portal veins.

5. By removal of the adrenals (1).

6. By trauma of the epigastric region.

7. By direct trauma of the stomach.

8. By artificially produced hæmoglobinæmia.

9. By anæmia produced by pyrodin.

10. By the ingestion of bacteria.

11. By intravenous injection of bacteria.

12. By intravenous injection of bacterial toxines.

13. By intravenous injection of mineral poisons and autolytic toxines.

14. By intravenous injection of adrenalin.

15. By injection of adrenalin into the wall of the stomach.

16. By cutaneous burns.

17. By artificially produced insufficiency of the pylorus and ingestion of the tripsin.

The above methods have been used singly or in the following combinations: (1) Joint resection of the vagus and sympathetic nerves; (2) trauma and ingestion of 0.5 per cent hydrochloric acid; (3) trauma and anæmia produced by graduated bleeding; (4) trauma combined with bacterial infection; and (5) resection of the cervical spinal cord combined with injection of 0.5 per cent hydrochloric acid.

It must be borne in mind that whereas some experiments yield positive findings, control experiments often give negative results. This has been especially true of the experiments dealing with the disturbance of the vagus or the sympathetic nervous system.

It will be readily understood that with the extensive experimental material at their command, the defendants of any given theory could easily cite facts apparently proving their conception to be correct, while the opponents could as easily collect contradictory evidence. Hence no theory has gained general acceptance since no conclusive evidence could be brought forward in any one single case. To make evidence conclusive, gastric ulcer has to be reproduced in animals.

As far as is compatible with the peculiar morphology of the species, the lesion created must be a destruction of tissue identical in animals, in so far as anatomic and pathologic structure is concerned, with acute and chronic ulcer in man.

The pathogenetic problem. The lesion must occur under conditions similar to those needed for the formation of ulcer in man. Under normal conditions, the vitality of the gastric mucosa is directly dependent on three factors: secretion, circulation, and innerva-

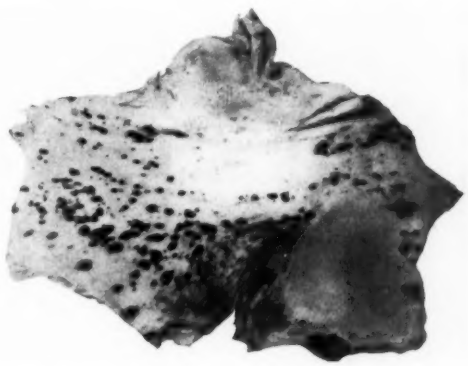

Fig. 1. Rabbit's stomach six hours after resection of left middle splanchnic nerve. Extensive hæmorrhagic condition of mucous membrane.

[1] Read by invitation before the American Surgical Association, Rochester, Minnesota, June 9, 1915.

Fig. 2. Hæmorrhagic lesion of mucous membrane from blood-vessels of muscularis mucosæ. Rabbit's stomach two hours after resection of left small splanchnic nerves. (X60.) Hæmatoxylin-eosin stain.

Fig. 3. Hæmorrhagic lesion from violent rupture of the blood-vessels of muscularis mucosæ and destruction of the mucous membrane. Rabbit's stomach two hours after resection of right and middle splanchnic nerve. (X60.) Bensley's stain for zymogen granules.

tion, the latter being the result of the two former, inasmuch as the secretory glands are stimulated by nerve impulses and food supply, through their innervation and blood-vessels. In order to obtain a "clean experiment," we must create a disturbance in one or more of these three fundamental factors, thus attacking the life of the cell at its very roots.

Secretion. The pathogenetic value of the gastric juice (if the latter can be considered a cause of gastric lesions through autodigestion of the mucosa) is by no means clear. This may be the result of one-sided conceptions. Faulty clinical deductions, stating that gastric ulcer must be accompanied by and originate from hyperacidity, have suggested the following series of experiments: (a) Giving hydrochloric acid by mouth over a prolonged period; (b) the use of subcutaneous injections of hypertonic sodium chlorid solutions intended to increase the actual amount of hydrochloric acid in the gastric juice.

Only negative results were obtained by these methods which were bound to result in failure, since the premise that acute digestion is the result of hyperacidity is itself based on misconception. If we are to accept the theory that destruction of tissue can be caused by autodigestion, more accurate knowledge of the actual chemical value, possessed by each of the various components of the gastric juice, should lead us to attribute these lesions of the mucosa either to an excessive production of peptic or to an insufficient quantity of antipeptic ferment.

Both hyperacidity and hypo-acidity are met with in gastric ulcer and should rationally be considered useful and natural measures of defense, counterbalancing the corroding effects of the pepsin, since Pavlow's experiment has proved that *in vivo* as well as *in vitro* the activity of pepsin is inhibited both by hyperacidity and hypo-acidity.

If any influence on the course of gastric ulcer can be ascribed to the gastric juice — and we may readily conceive that it cannot be entirely without effect since gastric ulcers appear in that part of the digestive tract which is constantly brought into contact with the gastric juice, or in places that have been artificially put under similar conditions (gastro-enterostomy) — we are logically bound to attribute this influence to the action of the gastric ferments, whose chemical activity has not thus far been clearly demonstrated.

Circulation. Among the experiments aiming at the reproduction of gastric ulcer through disturbed circulation, those blocking the minor vessels of the gastric mucosa by

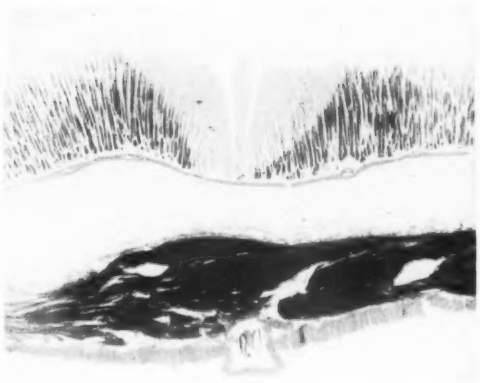

Fig. 4. Spastic condition of the blood-vessels of muscularis mucosæ. Incipient necrotic area in the mucous membrane. Rabbit's stomach six hours after resection of left middle splanchnic nerve. (X60.) Bensley's zymogenic stain.

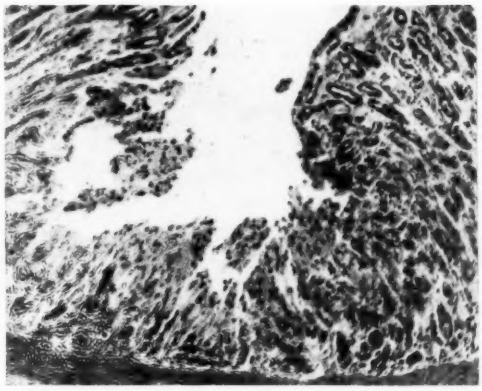

Fig. 5. Ulcer, healing by proliferation of surface mucous cells. Rabbit's stomach 25 days after resection of all right splanchnic nerves. (X130.) Mucin stain.

means of embolism have given the most satisfactory results. No results have been obtained by obstruction of the larger gastric and duodenal vessels. The following explanation seems admissible for the phenomenon: the larger vessel can re-establish a sufficient circulation by means of collaterals; the small vessels, on the contrary, though they cannot be called "terminal" in the true anatomical sense are in reality "terminal" from a functional point of view, and are incapable of supplying a sufficient collateral circulation.

The formation of gastric ulcer on the basis of embolic obstruction in the minor vessels of the gastric mucosa has proved conclusively that a disturbance of circulation in these vessels is in itself sufficient to produce typical circumscribed necrosis of the mucous membrane; the necrotic area thus formed is conical in shape, its base being nearest the surface, and presenting, after removal of the slough, the true picture of gastric ulcer. Ulcers thus produced are, as shown by the initial lesion and by their subsequent development, an exact replica of only acute human ulcer. They end in the formation of a scar with a complete regeneration of the mucosa. at least in such animals as survive operation for a sufficiently long period. Every attempt at thus reproducing chronic ulcer has resulted in failure. If, as has been shown, the pathogenesis of acute ulcer may be explained by circulatory disturbances of embolic origin, this explanation has proved inadequate to solve the problem of the origin of chronic gastric ulcer.

Innervation. Physiology has not yet clearly established what phenomena in the various phases of gastric motility and secretion are to be attributed to the influence of the vagus or the sympathetic nerves respectively. This is probably due to the fact that both systems of innervation are so intimately associated, that it is practically impossible to stimulate the one system by itself and prevent the action of the stimulus from being transmitted to the other.

Recent investigations have shown that both systems of innervation are equally involved in the regulation of secretion and motility, both exerting an exciting and restraining influence at the same time.

The sympathetic nerve, moreover, apart from the functions in which it co-operates with the vagus, also controls the circulation of the vasomotor nerves of the stomach and carries impulses of profound sensibility to the central nervous system. Owing to the part which the sympathetic nerve plays in the nutrition of the gastric mucosa, by regulating its circulation the title of "trophic nerve" is applicable to it in the most literal sense.

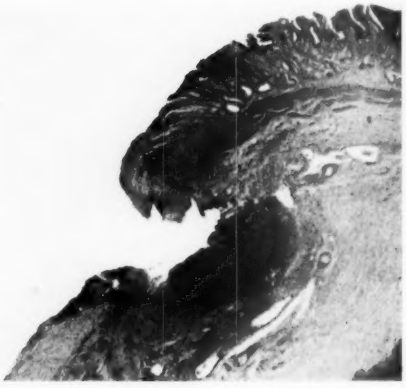

Fig. 6. Small typical callous ulcer in the pyloric region. Both edges are composed of young proliferating connective tissue. No trace of epithelial regeneration. Dog's stomach 35 days after resection of all the three left splanchnic nerves. (X60.) Weigert-van Gieson stain.

Fig. 7. Large callous ulcer in the pyloric region of same specimen as Fig. 6. (X70.) Safranin stain.

As has already been stated, attempts to reproduce gastric ulcer by means of disturbed innervation results in a great diversity of findings; and if positive and negative results cannot actually be said to contradict each other, at least the latter contain many new suggestions for the unravelling of the problems in question.

Although lesions presenting all the anatomical features of acute human ulcer could be produced, it did not seem possible to obtain the true chronic form. The only description of artificial ulcers, presenting anatomical features of chronicity and produced by disturbed innervation, may be found in Dalla Vedova's (2) monograph; these were obtained either by injecting alcohol into the splanchnic nerves; or by resecting these nerves after laparotomy.

Personal findings (3). Dalla Vedova's method suggests the following criticism: Ulcers forming after a laparotomy has been done cannot be said to be the direct result of nerve-resection only, as the manipulations needed to reach the nerves are bound to disturb and damage the surrounding viscera. It need hardly be emphasized that the operative technique is of primary importance in experiments of this kind, but even with faultless technique the fact remains that lesions which, under normal conditions of circulation and innervation, might be of little consequence, are bound to give rise to severe complication when the nerves themselves have been tampered with. To defend my experiments against these very valid objections, I have chosen the lumbar route for operation and attacked the splanchnic nerves extraperitoneally with one incision in the middle space of the costovertebral angle. This method, though by no means easy, excludes all damage to the viscera, and also enables one to resect the large, the medium, or the small splanchnic nerve individually. I have used dogs and rabbits for my experiments, with a view to comparing the results to be obtained in animals presenting different types of morphologic evolution and dependent on a different diet for nutrition.

The following results were obtained after resection (75 experiments) of the right and left splanchnic nerves:

1. Neither subsequent hæmorrhagic nor necrotic lesions were found to occur after resection of the major splanchnic nerve during a period of observation lasting from one to one hundred twenty-five days. Immediately after operation, however, signs of congestion might be seen in the gastric mucosa which cleared up in about ten or twelve days. Slight atrophy of the gastric cells, more particularly of the zymogenic cells, remained.

2. Resection, or ligation by means of silk thread, of the medium splanchnic nerve

invariably caused numerous circumscribed hæmorrhagic lesions side by side with non-hæmorrhagic lesions, presenting the characteristics of simple necrotic degeneration. These lesions we have found in the "cardiac pouch" in rabbits and in the pyloric region in dogs. Hæmorrhagic lesions of the pylorus and duodenum are rare in rabbits, while duodenal lesions are rare in dogs.

3. Resection of the minor splanchnic nerve occasionally resulted in slight hæmorrhagic lesions in the above-mentioned regions.

4. Simultaneous resection of both medium and minor splanchnics caused lesions identical with those already mentioned.

5. Combined resection of the three splanchnic nerves produced lesions identical with those described for the medium branch, only more pronounced in character.

6. Whenever the medium splanchnic nerve alone was resected or ligated, signs of hæmorrhage and intense congestion of all the blood-vessels were seen in the adrenal of the corresponding side, in both medulla and cortex; but those changes did not occur if the major splanchnic nerve alone was resected.

Macroscopically, the hæmorrhagic lesions produced by resection of the medium splanchnic nerve have the appearance of small dark specks which are sometimes grouped together so as to form circular hæmorrhagic areas from five to ten millimeters in diameter. These areas may be seen a few hours after operation (Fig. 1). In the various stages of their development the initial lesion appears to be due to a minute lesion in a blood-vessel of the muscularis mucosæ; from this point the hæmorrhage spreads, infiltrating and destroying the mucosa. The hæmorrhagic area becomes conical in shape, its base coincident with the surface of the mucous membrane (Fig. 2).

Sometimes the force with which the hæmorrhage starts is so great that its mere mechanical action suffices to rupture all the layers of the gastric mucosa as seen in the stomach of a rabbit which died about six hours after operation (Fig. 3). The two varieties of hæmorrhagic lesion; i.e., hæmorrhagic specks and groups of these, heal without any apparent connective-tissue reaction, through regeneration of the gastric mucous epithelium, the latter growing down along the edges of the ulcers and lining the cavities (Fig. 4).

In lesions resulting from direct injury to the mucosa, healing is far more rapid. In these the epithelization of the ulcerous cavity is not complete even twenty-five days after operation. This seems to justify the conclusion that disturbed innervation not only causes circumscribed hæmorrhages but also results in a slight alteration of the entire mucosa. Careful observation reveals the histologic features to consist in a slight degree of atrophy of all the cells, especially of the zymogenic cells and a certain amount of distortion in the formation of gastric glands. This points to a process of retarded regeneration.

As stated above, necrotic areas as well as hæmorrhagic lesions are found in these experiments. The former are few in number and show macroscopically as small round pale areas. Their lack of color causes them to stand cut sharply against the congested mucosa. Serial sections show these necrotic areas to have exactly the same shape as the hæmorrhagic lesions already described (Fig. 5). They do not, however, contain the slightest vascular lesion nor show any sign of extravasation. Careful study of their subsequent course has led me to believe that they are the first stage of a specific kind of ulcer which I am about to describe and which presents all the characteristic features of true chronicity.

The gradual development and terminal stages of these ulcers can be traced with great accuracy in experiments on dogs. The accompanying photomicrographs (Figs. 6 and 7) show two ulcers taken from the pyloric region of the same dog which died thirty-five days after resection of the three left splanchnic nerves. The lesions involve the mucosa and submucosa as far down as the muscular stratum; they show signs of infiltration and necrosis; no trace of epithelial regeneration can be found; the edges are covered with young connective tissue. Besides these ulcers, other lesions may be seen in the pyloric region, the latter all completely healed through a process of complete epithelization.

In these no connective-tissue reaction whatever can be observed. The results obtained offer the following points of discussion:

1. *Character of the ulcer.* As has been seen, disturbed innervation alone, without any additional trauma or infection, will suffice to create in animals lesions presenting all the essential characteristics of acute and chronic ulcer in man. These results are, of course, comparable only as far as their morphologic and histologic similarity is concerned. Clinical observations must need be valueless in dealing with different species. Comparison is made further impossible by the fact that animals survive these operations for a short time only and the lesions, being very extensive, are likely to be complicated by changes of metabolism. As we find chronic and acute ulcers in the same region of the same stomach, both originating at the same time, there is reason to assume that time does not play a paramount part in the process; i.e., that acute lesions do not take on chronic form, but that both varieties occur simultaneously and start as specific entities. Moreover, as both small and large chronic ulcers will be found in the same stomach, it is apparent that the size of the ulcer cannot be responsible for its insufficient healing.

2. *The origin of the ulcer.* A systematic study of the results obtained after resection of each splanchnic branch by itself seems to indicate that these nerves do not play identical parts in preserving the integrity of the mucous membrane. Resection of the major splanchnic nerve, although causing temporary paralysis of the gastric vessels is not in itself sufficient to produce permanently destructive lesions. The lesions obtained can only be compared with those resulting from resection of the medium nerve. At first sight this diversity of action seems contradictory; it is explained by the different degree in which the two nerves influence the blood-pressure. It has shown that more telling effects may be obtained by stimulating the medium splanchnic nerve than are seen after stimulation of the large splanchnic nerve, even though the latter control the larger field in abdominal circulation, faradic stimulation being used in both cases. This apparent contradiction is easily explained by the fact that the medium splanchnic innervates the adrenals; stimulation results in an increased secretion of adrenalin and, as the adrenal secretion has a physiologic as well as a selective action, it is one of the most powerful means by which contraction of blood-vessels can be produced. The results which I have obtained after resection of the medium splanchnic nerve only seem to illustrate the influence of this nerve on the adrenals, both by the rapidity (few hours after the lesion) with which the lesions appear and on account of the hæmorrhages by which they are accompanied. Overstimulation, rather than insufficient innervation, seems to be the principal cause, for it must be remembered that intravenous injection of adrenalin has proved conclusively that by increasing the adrenalin content of the blood, hæmorrhage can be produced in the gastric mucosa.

3. *The non-hæmorrhagic lesion.* To what cause are we to attribute the formation of the other, non-hæmorrhagic lesions? It does not seem logical to assume that they are due merely to circumscribed trophic disturbances: if this were the case, they ought to be found principally after resection of the major splanchnic nerve, and they are not. The following explanation seems to me admissible: namely, that we are dealing with spastic disturbances, due to the action of adrenalin and that whereas this action causes rupture of the blood-vessel in some points it leads only to spastic contraction in others. Klebs has already proved himself a warm defendant of the idea of "vascular spasm," which, however correct it may be, is unfortunately beyond conclusive proof as it cannot be made visible. By its very nature spastic contraction of a small blood-vessel remains a functional disturbance and does not leave visible traces on the arterial wall.

SUMMARY

1. The peripheral innervation of the stomach can be said to be "trophic" in its action as it regulates circulation and stimulates secretion, besides transmitting impulses of profound sensibility.

2. Insufficient innervation of the gastric mucosa can be traced only after some time by

a slight atrophy of gastric cells. This fact may be explained by congestion and by a deficit in secretory impulses as the latter, in accordance with the laws of biology, are known to act as stimuli of nutrition and growth.

3. Trophic disturbances are not in themselves sufficient to cause ulceration, unless accompanied by vascular disturbances resulting in hæmorrhage or spastic contraction of the vessels.

4. Ulcers produced by resection of the vagus cannot be explained if we do not take into account the vasomotor disturbance by which they are accompanied. If the vasomotor disturbances accompanying them are duly taken into account, they may readily be explained by the transmission of nervous impulses to the sympathetic fibers contained in the vagus and by the numerous anastomoses existing between the two nerves which cause the stimulus to be transmitted from one nerve to the other.

5. Acute and chronic ulcers produced by resection of the splanchnic nerves develop with great rapidity; this is due to the fact that the operation irritates the nerves of the adrenal medulla in consequence of which greater quantities of adrenalin are forthwith secreted. The adrenal secretion stimulates the sympathetic nerve fibers, controlling the non-striated muscles of the blood-vessels, thereby causing the formation of hæmorrhagic and spastic lesions. Whereas the hæmorrhagic lesion, presenting the essential features of acute ulcer, heals by means of a scar, the spastic lesion becomes the starting-point of genuine chronic ulcers.

6. Symptoms of deficient innervation appear only after specific characteristics of both types of ulceration are fully developed. Consequently nervous disturbances cannot be considered the primary cause of gastric ulcer, although it must be admitted that disturbed innervation plays some part in the subsequent development of the ulcers.

7. By resection of the splanchnic nerves ulcers may be produced in animals of which the histologic picture contains all the essential features of acute and chronic gastric ulcer in man.

THE ETIOGENETIC PROBLEM

Having reviewed the pathogenetic features of gastric ulcer and the numerous theories brought forward to explain them, the question remains to be discussed: Whether experimental work can be said to have furnished new suggestions corroborating or refuting the various conceptions of the etiology. It does not seem logical to assume that gastric ulcer should be caused by a single etiologic factor only, since we find it to be associated with the most widely divergent clinical syndromes, with symptoms of melæna neonatorum in infants, with trauma of the epigastric region, nephritis and uræmia, burns, sepsis, toxæmia, oligeomia, bacterial infections, incarcerated hernia, tabes, malaria, tuberculosis, and lues. In the majority of cases, however, ulcers appear spontaneously; no apparent relation to other diseases can be traced. This type of ulcer, which exhibits all the most typical features of the disease, presents the greatest problems to scientific investigation; its etiology is of paramount importance. On the edges of some of these ulcers which had all the characteristics of true chronicity, and for whose formation neither clinical nor anatomical causes could be found, colonies of bacteria were discovered by Boettcher. The hypothesis contending that gastric ulcer is produced by the cytolytic local activity of bacterial toxine is based upon this observation. Other explanations of the fact seem, however, equally admissible; the presence of bacteria may as logically be considered the result as the cause of gastric ulcer, and the contention seems justifiable that the presence of bacteria in the wall of the stomach is merely an evidence of subsequent infection, since disturbed nutrition itself creates lessened resistance. Experimental work was brought to bear upon the question. Attempts were made to produce ulcer by feeding animals both with toxins and bacteria. The lesions thus created did not in any single instance possess the characteristic features of acute or chronic ulcer in man; the ulcers produced appeared to be mere foci of infection starting in the lymph-follicles of the gastric mucosa. Rosenow (4) alone succeeded in reproducing ulcers of the genuine human type by streptococci from human ulcer.

If the results obtained in experimental work do not exclude the possibility from an etiologic point of view of ulcers forming in consequence of bacterial infection (as the clinical observation of Boettcher and the experimental work of Rosenow seem to indicate) the fact remains none the less that bacteria are found in a limited number of cases only.

Owing to the important part played by nervous disturbances in the experimental formation of gastric lesions, ulcer appears, in the majority of cases, entitled to a place among the morbid causes due to a central and peripheric or anatomical factor. I have mentioned the central factor because, as is well known, excessive psychic stimuli are capable of so changing the normal vasomotor tonus that vascular disturbances culminating in rupture of the small arterial walls may be caused in any part of the body — a fact which may be explained by the close association, both in anatomy and function, of the sympathetic nervous system and cerebrospinal tract.

The peripheral or anatomical factor must be taken into especial account since toxic stimuli — whether due to bacterial, to chemical, or biochemical agents — are capable of producing irritations in the sympathetic system, entirely comparable with those I obtained by means of surgical interference. *In other words, ulcer may be produced by any agent capable of damaging the sympathetic nervous system as it is on the integrity of this system, which controls circulation, secretion, and profound sensibility in the stomach, that the very life of the gastric cell may be said to depend. The theory of "trophic ulcer" must be taken in this sense.*

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METASTATIC CARCINOMA OF THE OVARIES

By William S. Stone, M.D., New York

THE ovary has long been regarded as one of the frequent primary sites for the occurrence of malignant neoplasms, but until the beginning of the present century little attention was directed to the possibility of frequent secondary deposits in this organ, except as they appeared to be part of a general metastasis in the terminal period of the disease. In the American literature there appears to be scanty evidence that either pathologists or surgeons have accepted the newer conclusions which have been expressed in quite an extensive foreign literature. It is the purpose, therefore, of the present writer to review this literature, and to add some material which he has examined in the Pathological Department of the Cornell University Medical College.

While some differences of opinion were evident prior to 1900, metastatic carcinoma of the ovary was, in general, considered to be of little pathological or clinical importance. Rokitansky (1) had observed, at times, cancer of the ovary as secondary to cancer of the uterus, breasts, and stomach. Billroth (2) said that his experience agreed with that of others that secondary cancer of the ovaries rarely occurs. Birch-Hirschfeld (3) and Olshausen (4) also concluded that it was of rare occurrence. Zahn (5), in reporting some rare forms of tumor metastasis, expressed the belief that, while the ovary is frequently the seat of cancer, it is rarely the seat of a metastatic growth. In the pathological institute at Genf, during the decade from 1877 to 1887, he found only four cases: three as regionary extensions from the uterus, and one as a metastasis from a distant organ, the breast. Leopold (6), however, noted the frequent association of malignant disease of the stomach with that of the ovaries without commenting upon their causal relations.

During the last decade of the nineteenth century a group of German writers, in their efforts to uphold the monocentric theory of the origin of cancer, showed a causal relationship in numerous instances between tumors which had previously been regarded as examples of the multiple appearance of primary independent growths. It was among these writers, apparently, that the literature relating to secondary cancer of the ovary began. Schimmelbusch (7), by showing the ease with which metastases may occur through the peritoneal lymphatics without giving gross evidence of their existence, materially reduced the number of apparently independent tumors of the abdominal organs. Bucher's (8) work suggests more emphatically than the other writers of this period the possibility of the frequency of secondary cancer of the ovary. He refers to nine cases in the literature, of which four were associated with carcinoma of the stomach, and five with carcinoma of the breast. Walter (9), commenting upon the simultaneous occurrence of cancer in paired organs, like the breast and ovaries, says that in the case of the breasts one tumor is surely secondary to the other, even if certain morphological differences exist, because modifications of histological structure are often noted in different parts of a tumor of the same breast. He thought it was more difficult to determine the relations in the case of bilateral tumors of the ovaries, but he concluded that the most common origin was the implantation of cancer-cells from the perforation into the peritoneal cavity of gastric or intestinal growths. Gebhard (10), in 1899, appears to be the first author of a textbook to express the view that secondary cancer of the ovary is probably more frequent than had hitherto been supposed. The ovaries, he says, seem to be an exception to Virchow's (11) dictum, that those organs which show a decided tendency to become the seat of protopathic tumor formation possess very little tendency to metastatic growth. An explanation, however, for the coexistence of tumors in widely separated organs, like the ovaries and stomach, or breast, he regards as impossible to make, because of our meager knowledge of the origin of cancer.

There appeared also during this period a

number of reports of cases in which ovarian tumors, diagnosticated as sarcomata or endotheliomata, were associated with carcinomata of other organs. Bode (12), for example, presented a case in which a double fibrosarcoma of the ovaries, with areas having an endotheliomatous structure, appeared after an operation for the removal of a pyloric carcinoma. Fleischmann (13) reported the finding of a cancer of the pylorus at autopsy four days after an operation for the removal of a double fibrosarcoma (myxomatodes). In the discussion of this case, Temesvary (14) reported an autopsy in which he had found a fibrosarcoma of the ovaries associated with a carcinoma of the stomach, peritoneum, and retroperitoneal glands. He stated that he had found, of 300 cases of ovarian sarcomata in the literature, 4 with similar associations — 3 of the stomach, and 1 of the colon — in all of which both ovaries were involved. Lovrich (15) reported a case of ovarian sarcoma associated with a gelatinous carcinoma of the rectum.

A new interest in the relation of these cases to metastatic cancer of the ovary was created by the work of Krukenberg (16), who, in 1896, described his findings in 5 cases, to 4 of which, at the suggestion of Marchand, he applied the name "fibrosarcoma mucocellulare (carcinomatodes)." The fifth case, although having numerous appearances that were similar to the others, he classified as an endothelioma. Krukenberg says of these tumors that they are apparently always bilateral and usually accompanied by ascites. The entire structure of the ovary is involved, forming a large tumor which preserves in general the shape of the normal ovary. It is essentially a solid tumor, of firm consistency in the periphery, less so, even soft, in the center, dense areas, however, alternating with soft myxomatous parts throughout its entire structure. The surface is sometimes distinctly lobulated. The dense areas show histologically an excessive spindle-cell growth of the ovarian stroma, justifying, he thinks, the diagnosis of a fibrosarcoma. In other less dense areas, due apparently to a mucoid degeneration, the stroma consists of a fine fibrillary meshwork, shading off into a distinctly myxomatous structure. Throughout the different areas large epithelial-like cells are seen in large or small groups, sometimes arranged in single or double rows like a scirrhous cancer. In the myxomatous areas they may present an arrangement of larger alveoli. The cells differ widely in their size and shape — from large rounded cells with a well-stained nucleus and a slightly swollen body to those in which the protoplasm of the bodies is so swollen from the mucoid degeneration that the nucleus is pushed to the side of the cell into a seal-ring shape. While appearing in certain areas to be of epithelial origin, Krukenberg says that he could nowhere find a connection between these cells and normal epithelial elements of the ovary. On the other hand, he believes the different forms of these cells appear to be simply transitional stages of mucoid degeneration of the stroma cells. Because of the extensive metastases in his first case, and particularly because of the similar character of the cells which he found distending the lymphatic vessels throughout the body, he is not definitely certain they are not carcinomata. The importance of Krukenberg's description and interpretation of these tumors appears in all of the subsequent discussion of the subject of metastatic ovarian cancer.

After an interval of five years from the time of Krukenberg's publication, during which little confirmation of his conclusions is found, Schlagenhaufer (17), in 1902, made a notable contribution both to the interpretation of Krukenberg and to the entire subject of secondary cancer of the ovary. He collected and tabulated 71 cases from the literature, adding 8 cases of his own, as follows: 61 with cancer of the stomach; 7 with cancer of the gall-bladder; 1 with cancer of the suprarenal gland. He directs attention to the clinical features and discusses their histological structure. Clinically, he observed that the ovarian tumors were almost invariably so large as to practically control the clinical picture. At operation, he says, the coexistence of a tumor in another organ was often not discovered, and even later the clinical signs of tumor were usually ascribed to metastatic recurrences from the

ovarian tumors. Tuberculous peritonitis had been the clinical diagnosis in several cases, and two had applied for treatment under the supposition that they were suffering from the vomiting of pregnancy. Both in his own cases and those from the literature, the clinical diagnosis had been invariably wrong. Regarding the pathology of these tumors, he interprets the "Krukenberg tumor," of which he had four cases, as of epithelial origin, the mucoid degeneration of the cells being a colloid degeneration because of their origin from primary growths of the gastric mucosa. He likewise included 15 cases of ovarian sarcomata or endotheliomata, as belonging to the class of secondary carcinomata of the ovary — the majority of the scirrhous type.

Since the publication of Schlagenhaufer's work the writer has reviewed the reports of 133 cases in the literature, in which the descriptions were sufficiently complete to indicate that a causal relationship existed between the ovarian and the tumors of other organs, and in which, with few exceptions, the tumors of the ovaries were undoubtedly secondary. The primary tumors occurred among the different organs, as follows: stomach (18) 75; breasts (19) 25; large intestine (20) 22; gall-bladder (21) 5; small intestine (22) 4; pancreas (23) 1; appendix (24) 1. In these reports numerous writers have discussed their occurrence and frequency, their clinical features, their pathology, and routes of metastasis.

FREQUENCY OF SECONDARY OVARIAN CARCINOMA

Bland-Sutton (25) says that he agrees entirely with Schlagenhaufer's conclusions, and that for twenty years he has been suspicious that bilateral cancer of the ovaries is frequently secondary, because he has noted the presence of massive deposits in one or both ovaries in 10 per cent of autopsies after mammary or gastric cancer. The majority of cases, he says, were operated upon under the impression that they were primary tumors, and the presence of a coexisting cancer of the gastro-intestinal tract was overlooked in spite of the presence of such typical signs as persistent vomiting and progressive emaciation. Bland-Sutton characterizes such errors as the result of an "occupation bias," by reason of which the pelvic surgeon allows the presence of a definite pelvic tumor to fill the foreground of the clinical picture, while the general surgeon, too intent upon a tumor of the stomach, will disregard the significance of enlarged ovaries. He has also frequently noted, as one of the remote results of operations for ovarian tumors, intestinal obstruction from an obturating malignant growth which has the typical characteristics of a primary cancer. Pathological reports alone, he deems as insufficient to determine the primary site, but they must be combined with a clinical history, giving assurance that from a careful examination a tumor of the gastro-intestinal tract may be excluded.

Glockner (26) found during the years 1901 and 1902, among 14 cases of ovarian cancer, 6 associated with a cancer of some other organ. From a study of 18 cases, he concludes: (1) Secondary cancer of the ovaries is relatively frequent. (2) Most of the bilateral cases are secondary, especially of the scirrhous variety (3). In the presence of a cancer of other abdominal organs, the ovarian cancer in the vast majority of cases is not primary, but a metastasis. He thinks the primary tumor occurs most frequently in the stomach, breasts, uterus, and gall-bladder. In his own cases, 9 occurred in the stomach, 5 in the breast, 3 in the uterus, and 2 in the large intestine.

Stickel (27), from a study of 13 cases, concludes: (1) In every case of primary cancer of the breast, stomach, gall-bladder, and large intestine, before an operation is undertaken, a thorough examination, especially of the ovaries, should be made. One must not disregard the possibility of their being affected because the peritoneum or retroperitoneal glands are not apparently involved. (2) If there is a suspicion that bilateral cancer of the ovaries exists, a most searching examination should be made for a primary cancer elsewhere. In the search for growths of the stomach or intestine, one must not be satisfied with palpation, for the primary

growth may be too small: every aid to diagnosis should be used.

Engelhorn (28) found in the Tuebingen clinic during the decade from 1897 to 1907, among 80 malignant tumors of the ovary, 13 which were associated with cancer of the stomach, and in all of which, he believes, the primary tumor was in the stomach.

Amann (29), from an observation of 13 cases, expresses his belief in the frequency of secondary ovarian cancer.

Goullioud (30) has met with 5 such cases, and considers that ovarian metastases are an important factor in the evolution of cancer of the stomach.

Pfannenstiel (31), who has been an ardent advocate of the frequency of the multiple appearance of primary cancer, says, in 1908, that he is convinced that in most cases of bilateral cancer of the ovaries, which are associated with cancer of the stomach or other organs, the ovarian tumors are secondary, and that he and Olshausen are wrong in their previous conclusions regarding the rarity of such metastases.

In spite of the fact that, from the writer's review of the literature, the breast appears to be the organ, next to the stomach, which is most frequently the primary seat, we find little discussion of its occurrence. Coupland (32), however, in 1876, among 80 mammary carcinomata, found 6 per cent with ovarian metastases, and Toerek and Wittelshoefer (33), among 366 cases, found 7 per cent. Handley has confirmed these statistics, showing among 422 cases 6.7 per cent with ovarian metastases. His statistics are based upon the autopsy records of two hospitals, in one of which, as a special provision was made for cancer patients so that they remained throughout the course of the disease, the findings represent, in general, later stages of the disease. No such provision was made in the other hospital, and the records are mostly those of patients who have generally died at an earlier period in the evolution of the disease. His cases were, therefore, designated as "early" and "late," and certain differences in the percentages of invasions in the internal organs suggest some new facts. Of the "early" cases the ovarian metastases were present in 4.8 per cent, while in the "late" cases they were present in 8.6 per cent. He found, furthermore, that, in the "early" cases, thoracic metastases alone were present in 10 per cent, and in the abdominal organs, without thoracic invasion, in 17 per cent; while, in the "late" cases, thoracic invasion alone was present in 22 per cent, and in the abdominal organs alone in 11 per cent. There were 53 cases, or 12.5 per cent, in which the invasion of the internal organs was limited to those strictly within the peritoneal cavity; and of these the liver was involved in 84 per cent, the ovaries in 11 per cent, the tubes in 2 per cent. In 2 of the 53 cases the ovaries alone were involved. Of 8 cases of multiple abdominal metastases, those in the liver were associated in five instances with a growth only in the pelvic organs. Handley's statistics agree with those of the older writers in the fact that, next to the liver, the ovaries are the most frequent sites among the abdominal organs. The peritoneum in Toerek and Wittelshoefer's series showed involvement in only 5 per cent, while the abdominal lymph-nodes, showing a percentage of 9.5, slightly in excess of that of the ovaries, were undoubtedly, as Glockner (26) suggests, in numerous instances tertiary extensions from the liver, ovaries, or other abdominal organs in which metastases had already occurred. A suggestive comparison is also furnished in the statistics of Toerek and Wittelshoefer, which show the supraclavicular and cervical lymph-nodes to be involved in a percentage of 6.3, slightly less than that in the ovaries. Sitzenfrey (35), who had been impressed with the clinical frequency of ovarian metastases in mammary cases before the appearance of Handley's work, suggested a possible additional therapeutic advantage in the performance of the Beatson operation.

Regarding the occurrence of secondary mammary cancer from primary abdominal tumors, there is little in the literature to suggest that it is more than a rare event. Plew (36) has collected six cases from the literature and added one of his own, but the data which he gives do not suggest a definite conclusion.

THE PATHOLOGY AND HISTOGENESIS OF SECONDARY OVARIAN CARCINOMA

The discussion of the pathology of these tumors is found to be closely related to the interpretation of the histogenesis of the Krukenberg tumor. Wagner (37), almost simultaneously with the publication of Schlagenhaufer's work, reports a case of malignant tumor of both ovaries as secondary to a cancer of the pylorus, in which, he says, the histological structure of both the ovarian and the pyloric tumors was typical of scirrhous cancer, with well-marked colloid degeneration of the cells. From the similarity of their structure to that of the Krukenberg tumor, he agrees with Schlagenhaufer that the latter is a secondary and not a primary tumor, deriving its characteristic growth of mucoid cells from its origin in the gastric mucosa. The same interpretation is given more decisively by Ulesko-Stroganoff (38) in the records of three similar cases. She expresses doubt as to the primary nature of Krukenberg's first case and the one reported by Schenk (39), both of which are generally accepted as primary. Wermuth (40), in discussing ovarian sarcoma and its complications, says of the Krukenberg tumor that it shows a mixture of epithelial and connective-tissue cell growth, representing a metastatic cancerous invasion, to which the ovarian stroma reacts with a sarcomatous proliferation. Amann (29), in his work upon secondary ovarian cancer, refers to 15 cases in the literature, almost all of which he regards as metastatic colloid carcinomata from a carcinoma of the stomach or intestine. Among such cases, he says, are several endotheliomata or sarcomata, which are instances of secondary cancer. He reports 4 cases of Krukenberg tumor of his own as secondary. Stickel (27), also, from the similarity in the structure of several of his cases of secondary ovarian cancer to that of the Krukenberg tumor, believes it is a metastatic tumor. Glockner (41), in his contribution to the pathology of solid ovarian tumors, describes a typical Krukenberg tumor, which appears undoubtedly to be primary, and in which the mucoid cells are most probably derived from the stroma cells of the ovary. He does not regard, however, such cells as specific for a certain form of tumor, as he has found similar cells in ovarian tumors that were secondary to a cancer of some other organ. He also describes mucoid cells in other cases of primary ovarian tumors, particularly in one which he designates as an endothelioma which he acknowledges may be easily confused with the carcinomata, sarcomata, or Krukenberg tumor. The conclusion, he says, seems warranted that the ovary, in both its epithelial and its connective-tissue cells, possesses a great tendency to mucoid degeneration. Pfannenstiel (31) says that many of the Krukenberg tumors, including some of those reported by Krukenberg himself, were undoubtedly secondary to intestinal carcinomata. Bondy (42) reports 4 cases of undoubted metastatic cancer of the ovaries, which, in part, have the structure of a Krukenberg tumor, and in part that of an endothelioma. Fischer (43) describes two Krukenberg tumors, both of which he regards as primary. Cohn (44) records 4 cases, 2 of which were secondary to a cancer of the pylorus, and the others were also probably secondary. In the American literature we find the record of a case by Schwarz (45), occurring in a patient 30 years of age. Both ovaries were involved, and she died without clinical evidence of intestinal disease. The failure to obtain an autopsy in the case of Outerbridge (46) also makes its origin uncertain. He carefully describes the histological features of his case, showing by the use of different stains for mucus that the cells are derived from those of the stroma, and, therefore, designates the tumor as a fibrosarcoma undergoing myxomatous degeneration. The striking similarity in the histology of certain forms of primary ovarian cancer to that of the Krukenberg tumor is quite definitely demonstrated by Gebhard (10) in his description of a group of primary ovarian cancer, which he designates as a "diffuse carcinoma." In this group, he says, the distinctly alveolar arrangement is to a great extent lost and more of an embryonal condition becomes evident by a closer blending of the epithelium and connective tissue. The epithelial elements are arranged so ir-

regularly in the bundles of connective tissue that they present pictures remarkably like those of a sarcoma. Under a high power, however, the epithelial nature is evident, and in certain areas the arrangement is more regular, so that a small alveolar structure is manifested in which the lumen is often filled by swollen, transparent cells with the nuclei pushed to their peripheral edge, furnishing often an appearance of primordial follicles. In the stroma there are also found degenerative changes. This description seems to the writer to be especially suggestive because Gebhard makes no reference to the interpretation of Krukenberg.

Numerous writers have attempted to distinguish the pathological anatomy of the secondary tumors from that of the primary. Amann (29), using as a basis his observations in 18 cases, describes three types of metastatic cancer of the ovary: (1) Œdematous fibromata, with epithelial infiltrations which are often sparsely diffused as compared with the marked growth of connective tissue, presenting adenocarcinomatous or carcinomatous columns, the cells of which frequently show a colloid degeneration resembling that of a carcinoma of the gastro-intestinal tract. Amann records 6 cases of this type, in which the excessive growth of connective-tissue cells represents a fairly constant reaction of the ovarian stroma to the infiltrating cancer-cells, as noted also by Krauss (47), Schlagenhaufer, Polano (48), and Glockner (26), and to which has been ascribed the enormous size of these tumors as compared with the small primary growths in the other organs from which they are derived. Amann says that the cellular growth of the stroma is especially marked in the peripheral areas, while the œdematous changes are more extensive in the central parts. But even in ovaries, scarcely changed macroscopically, as, for example, in a case secondary to a primary mammary cancer, he noted small adenocarcinomatous foci surrounded by a shell of strongly growing connective tissue. (2) A nodular medullary type, consisting of more or less solid nodes of an adenocarcinomatous structure. (3) Cystomata, with scattered deposits of a fibrocarcinomatous structure. In the two latter types, Amann says, there is often also a marked œdema of the connective-tissue areas, and expresses the opinion that, because of this reaction of the stroma, much of the confusion has arisen relative to the diagnosis of certain sarcomata and endotheliomata. With this view Roemer (49) and Polano (48) agree, the latter designating numerous cases as "pseudo-endotheliomata."

The nodular type appears to be the characteristic form in which metastatic cancer of the ovary occurs. Gebhard (10) says it is most frequently located in the center of the ovary, at times in the form of multiple nodes, and that the carcinomatous masses appear more frequently than in other ovarian tumors, as long, narrow alveoli penetrating the ovarian stroma. Glockner (26) has shown in the cut-section of only slightly enlarged ovaries one or more circumscribed cancerous foci, which may appear, apparently, in any part of the ovarian stroma. Stickel (27), also, shows how such circumscribed nodes, recognized macroscopically, correspond in general, microscopically, to the cancerous areas, although cancer-cells may be seen infiltrating the tissues outside of the nodes. In 5 of Stickel's cases the tumors have reached a large size and the ovarian structure has become diffusely infiltrated. In other cases it is possible, according to the age of the metastases, to follow the advance of the cancerous invasion, from circumscribed foci to an increasing number of infiltrating paths, until finally the entire structure becomes involved. Cyst formation was noted in some of Stickel's cases, in one of which they were so numerous as to be designated as a cystadenocarcinoma. Pfannenstiel (31) says that metastatic carcinomata of the ovary regularly present features which distinguish them macroscopically from primary tumors. He says they are mostly dense, nodular tumors, of about the size of the fist, and in the majority of cases are double-sided (2 of his 3 cases). Their histology varies with that of the primary tumor and the age of the secondary growth. In the early cases, the epithelial infiltrations are few as compared with the growth of the stroma, in which they are embedded as small nests, or long, narrow, alveolar-like pro-

cesses, simulating, at times, the appearance of an endothelioma. Pfannenstiel confirms Amann's description of his first type, in which the growth of the stroma is so excessive as to appear like a fibroma, in the central parts of which the œdematous condition may give this area a soggy consistence.

The failure of both Glockner and Stickel, even in the early cases, to detect a proliferation of the normal epithelial elements of the ovary may be accepted as corroborative of their secondary nature, but the histogenesis of all ovarian tumors is frequently obscure, and in the advanced cases the histology alone will not permit of a differentiation between the primary and secondary tumors.

Most of the writers have satisfactorily shown a similar histological structure in the ovarian tumors and in those of the organs which they have concluded to be the primary site. Within certain limits, however, anaplasia, metaplasia, reversion, and various degenerative processes contribute to a well-marked variation in the morphological features of all ovarian tumors, thus accounting for much of the confusion that exists regarding their histogenesis. Kuester (50) describes two ovarian tumors which were associated with a cancer of the pylorus. The larger one contained a dermoid, and in both tumors were nodular growths containing three fairly well differentiated forms of carcinoma — colloid, large alveolar, and a scirrhus. He discusses their origin from the three layers of the dermoid, quoting in illustration a case of Yamagina, which originated from the presence of some atrophic mammary tissue, but concluded from the autopsy that in his own case the primary site was the pylorus. All of the forms, he says, however different they may appear, are a complex of gland cells, judged not by the morphological peculiarities of the individual cells, but upon their arrangement, which shows a clear tendency to gland formation, more or less complete in different parts of the tumors. In support of his conclusion, Kuester cites the opinions of Ribbert (51) and Borst (52) regarding the influence of tissue resistance and nutrition in modifying the structural appearance in the metastatic invasions of a highly differentiated carcinoma. The colloid degeneration, for example, occurred most extensively in areas where the connective-tissue septa are sparse and the vascular supply is poor. Roemer (49), noting a difference in the size of the cells in a gastric and ovarian carcinoma, says such a criterion of the causal relations of two tumors cannot in itself be absolute. Within certain limits the structure of the organ in which the cancer grows determines both its method of growth and the configuration of the cells. He says the presence even of necrosis may not be significant of the priority of the tumor, as he observed in a gland in which the tumor was secondary to a carcinoma of the œsophagus. Further indications of the difficulty of distinguishing primary and secondary ovarian tumors, histologically, are furnished by Goodall (53), who, from a painstaking study of comparative embryology, histology, and the function of the ovaries, has offered evidence to support the theory that all epithelial neoplasms of the ovary derive their origin from fœtal "rests," all of which represent metaplastic changes of invasions of the germinal epithelium, and contain tall columnar cells, goblet cells, true mucus cells, while still others have ciliated epithelium. Glockner (41), also, seems inclined to accept Walthard's (54) findings in normal ovaries at different ages of various "embryonal anlage," containing ciliated cells, beaker cells, and others, as indicating the origin of many epithelial tumors of the ovary.

In spite of the numerous difficulties, however, that present in the determination of the causal relations between tumors, it seems to the writer that the question of structural differences has been given sufficient attention to indicate the accuracy, in general, of the conclusions recorded in this literature. The criticism, therefore, by Outerbridge (46) of Stickel's conclusions as to the frequency of metastatic cancer of the ovary, does not appear to be justified. For example, in case 12 of Stickel's (27), in which a carcinoma simplex of both ovaries was evidently secondary to a similar tumor of the breast, there was also present an ulcerating adenocarcinoma of the ascending colon, which was undoubtedly primary. The case was therefore classed by

Stickel as one illustrating the multiple appearance of primary carcinoma. In fact, a definitely localized growth in either the gastro-intestinal tract or the mammary gland is easily identified by a gross examination, and it is evident that, after giving due consideration to the histology and the failure to discern proliferation of the normal epithelial elements of the ovary, the primary site of the tumor has been determined in a majority of the cases by the gross pathology of the neoplasms in the other organs.

The comparative frequency of the different forms of carcinoma in these cases is undetermined, but that a large number, both of those in the gastro-intestinal tract and of those in the mammary gland, were of the scirrhous variety, may partly explain the clinical prominence which the ovarian tumors have so uniformly occupied. A small, slowly growing scirrhus of the pylorus, for example, with few or no signs of its existence, finally metastasizes in the ovary, where under more favorable conditions it may assume a rapid and extensive growth.

All of the cases of metastatic cancer of the ovary, with few exceptions, have been found to be bilateral, many of them, however, giving little or no gross evidence of malignant invasion. The value of this as evidence of their secondary nature is diminished by the fact that primary ovarian tumors are also found to be bilateral in a large percentage of cases. The statistics show a variation from 25 to 50 per cent, but in these estimates secondary tumors have undoubtedly been included. The observations of Walthard (54) and Goodall (53), both of whom have noted that embryonal "rests," if present in normal ovaries, occur uniformly in both organs, also emphasize the necessity of withholding judgment regarding the value of bilateral involvement as evidence of a secondary nature.

THE ROUTES OF METASTASIS

The transmission of cancer from organs or tissues to distant parts of the body still presents one of the important problems of cancer research. Except for the recognition of local extension to neighboring structures through the lymphatics, little attention has been given to the route of its further invasion except as a chance distribution by embolic transportation through either the blood or the lymphatic vessels. In the literature of metastatic cancer of the ovaries, we find much of importance in the discussion by which metastases occur between internal organs, especially of the abdomen.

Retrograde transportation through the lymphatic vessels is accepted by Roemer (49), Glockner (26), Stickel (27), and Pfannenstiel (31), as the most probable route in the vast majority of cases. From a carcinoma of the stomach, for example, these writers and others have demonstrated a continuous course of lymphatic invasion through the lymph-vessels and nodes behind the stomach and pancreas into the retroperitoneal lymphatics along both sides of the aorta, to the enlarged lumbar nodes, from which, through a reverse current in the spermatic lymph-vessels, the cells are transported into the ovaries through the hilum. This route is shown to be the only probable one in many cases in which no peritoneal implantations are discoverable. Schaeffer (55) records a case to show that, as he thinks, a metastasis may occur along this route in the reverse direction.

Peritoneal implantation, as a route for the spread of cancer among the abdominal organs, was first suggested by Virchow (10), who said that, from a primary growth of the stomach, for example, which has reached the serous layer, multiple peritoneal nodes may be engrafted upon distant parts, particularly in the region of the pelvic pouches. Bucher (8) is credited with being the first to suggest this way as possible for metastatic invasion of the ovaries from growths in distant organs. The publication, however, of Krauss's (47) work, giving the pathological findings in 5 cases, and the results of his animal experimentation, created an extensive discussion of the subject. The description of the histology in his cases appears to show conclusively that small cancerous invasions have occurred through the ovarian surface; and, from the presence of minute colored particles in the cortical areas of the ovaries of animals, after a solution of India ink had been in-

jected into their peritoneal cavities, Krauss concluded that the germinal epithelium is particularly suitable for cancerous invasion. Wolffheim (56), however, in repeating the experiments of Krauss, did not confirm this conclusion. On the contrary, he concluded from his own findings that the germinal epithelium is remarkably resistant to the penetration of corpuscular elements, except at such places as had been injured by the bursting of a graafian follicle. Confirmatory of this opinion, he found an extensive penetration of the endothelial surfaces of the other abdominal organs and neighboring structures up to the line marking the existence of the germinal epithelium. The importance of Wolffheim's observations relates especially to the clinical fact, with which practically all of the observers *agree, that the age at which these metastatic tumors of the ovaries are found is during the period of the functional activity of these organs.* Sitzenfrey (57), for example, repeats the suspicions which he and Schenk had previously expressed that the operative results for carcinoma of the stomach, because of the possibility of this method of metastasis, might be improved by removing all ovaries, if the disease occurs while these organs are functionating. A case of Gottschalk (58), 55 years of age, showed two metastatic nodes in an ovary otherwise atrophic one year after an operation for cancer of the body of the uterus, but the metastases are most likely to have occurred by lymphatic extension through the hilum. Considering the number of cases recorded in which the histological descriptions are complete, it seems strange that a demonstration of invasions through the cortical layer of the ovaries has not been more frequently made. Even among Stickel's (27) early cases he did not find one, but they were not examined, he remarks, with the object of solving the question of peritoneal implantation. Glockner (26), also presented only one case, in which he demonstrated a lesion similar in every respect to the findings of Krauss. In this case a growth of the stomach, showing well-marked mucoid degeneration of the cells, had penetrated the serosa. Numerous peritoneal implantations were present, and the

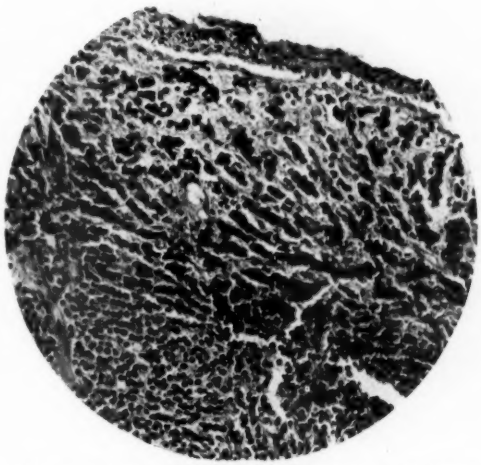

Fig. 1. Case 1, Embryonal carcinoma of the ovary. Alveolar structure in peripheral area.

ovarian surfaces showed in places the invasions of an adenocarcinomatous growth, with mucoid degeneration of the cells similar to that in the stomach. In some places small particles of similarly constructed cells were clinging to the ovarian surface. Sitzenfrey (59) describes similar findings in a case, 35 years of age, in which neither ovary gave gross evidence of the disease. Roemer (49) also records a case, 29 years of age, in which the ovaries and a puerperal uterus showed implantation metastases. The writer's review of Wolffheim's (56) observations suggests that the reason for the failure to demonstrate such lesions more frequently may depend upon the rapidity of the reaction of the ovarian stroma to the invasion of cancer-cells, and to their almost immediate inclusion by the processes incidental to the involution of the ruptured follicles. A microscopic penetration of the serosa in cases of a pyloric growth, for example, is suggested by Glockner (26) to account for peritoneal implantation in numerous instances in which there is no gross evidence of the extension to the peritoneal surface. Sitzenfrey (59) also suggests that in some cases a regionary extension to the omentum may not produce a gross lesion, but from its minute foci cancer-cells may be scattered throughout the peritoneal cavity.

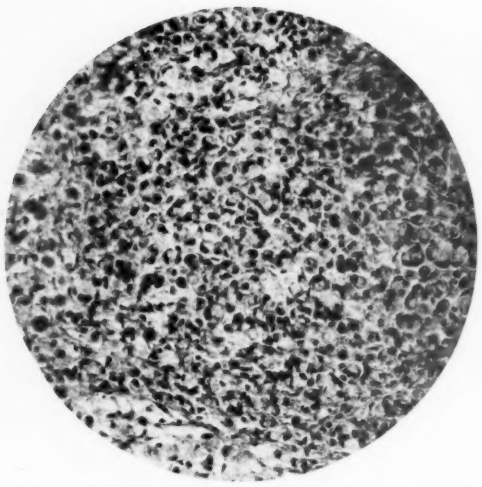

Fig. 2. Case 7, Krukenberg tumor of the ovary. Diffuse growth of epithelial cells in different stages of mucoid degeneration, mostly well advanced, showing the typical signet ring form.

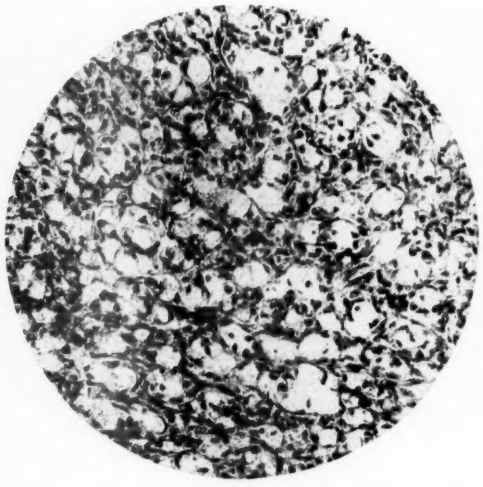

Fig. 3. Case 7, Krukenberg tumor of the ovary. More advanced stage of mucoid degeneration; the stroma also shows a reaction and the structure has a myxomatous appearance.

The presence of ovarian metastases without evidence of peritoneal implantation of other organs has been offered by several of the writers as a serious objection to this mode of metastasis. Regarding this question, one may point to the location of the ovaries in the lower part of the abdominal cavity, particularly their close relation to the pouch of Douglas, which Sitzenfrey (59) has designated as the sewer-trap, "Schlammfang," of the peritoneal cavity. Schnitzler (60) found in eleven cases of carcinoma of the stomach, for example, metastases in the anterior rectal wall just beneath the peritoneal layer. Rosenstirn (61) made examinations at the autopsies of 15 cases of malignant disease to determine the presence of implantation metastases in the pouch of Douglas—seven males and eight females. In the males none were found, but in five of the females they were present as superficial lesions just beneath the se ous layer, either at the bot om or in the anterior and posterior wall. In one case, the youngest, 35 years of age, in which the primary site was in the stomach, the left ovary showed an alveolar invasion of the entire ovarian structure. The right ovary was large and contained an excessive amount of connective tissue, but no evidence of cancerous infiltration. Peri-ovaritis and adhesions existed in the other cases. A case of Lubarsch is cited by Bucher (8) to show the protective action of such adhesions, one ovary only being the seat of cancer, the other being embedded in strong adhesions. In a case of Sitzenfrey (59) the only metastases outside of the ovaries were microscopic foci in the omentum and implantation nodes in the pouch of Douglas. Strauss (62) is so impressed with the possibility of the frequent presence of early metastases in the pouch of Douglas that he suggests that a pelvic examination in certain cases might be an aid in the differential diagnosis between a simple ulcer and a carcinoma of the stomach. Tilp (63), who has recorded a case with the primary site in the gall-bladder, says that the predilection sites for implantation metastases, after the growth has penetrated the peritoneum, are the pouch of Douglas, the vesico-uterine pouch, the insertion of the mesentery to the intestines, and the surfaces of the ovaries. Both the gross and the histological evidence is against either the hæmatogenous or lymphatogenous route of invasion.

Regarding primary carcinoma of the breast,

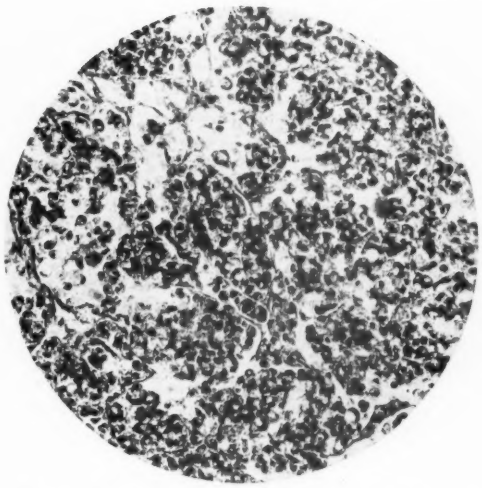

Fig. 4. Case 7, Krukenberg tumor of the ovary. An area in which a distinctly alveolar structure is seen.

Fig. 5. Case 10, Implantation metastases upon the cortical surface of an atrophic ovary. Detached fragments of the tumor-cells.

of 9 cases which Glockner (26) and Stickel (27) record, there were 5 in which neither enlarged lymph-nodes nor peritoneal implantations gave gross evidence within the abdomen of the route by which the ovaries had become invaded. In one case the only other abdominal metastases were nodes in the liver and the pouch of Douglas. Both authors seem inclined to exclude peritoneal implantation as the mode of metastasis, and fall back upon embolic transportation through the blood as the most probable explanation. Bland-Sutton (25) is the only writer to refer to Handley's interpretation of the routes of extension between mammary and ovarian tumors. If we accept Handley's (34) histological findings, that a mammary cancer spreads by lymphatic permeation through the deep fascial plexus to the epigastric triangle and thus permits cancer-cells easily to invade the peritoneal cavity, the theory of implantation to the organs and structures of the lower abdomen presents the same degree of probability, as a frequent route of metastasis from mammary tumors, as it does from carcinoma of the stomach or gall-bladder. His observations are especially suggestive regarding metastases in these organs after operations for mammary cancer — that the modern operation protects the thoracic viscera from subsequent invasion more frequently than it does the abdominal organs.

In connection with this review of the subject of metastatic cancer of the ovaries, the writer has examined the following material:

Case 1. Embryonal carcinoma of the ovaries. Primary site, probably in ovary; rapidly growing; general metastasis of abdominal organs by invasion through peritoneal surfaces; metastases in breasts; thoracic organs apparently free from metastases.

Clinical history. A young woman had complained of a rapidly growing tumor in the right breast, which was first noted two months prior to her admission to the hospital. She had had three children and one miscarriage, which occurred two months before the tumor in the breast was first noted. Menstruation, which had last appeared five days prematurely, had otherwise been normal.

Physical examination. A large, fairly well nourished woman. The right breast was enlarged to three times the size of the other. There was no superficial evidence of inflammation. The nipple was erect and protruding. In the lower, outer third was a large mass, which was firm and movable over the deeper structures, and the skin was not involved. The glands in the axilla were definitely enlarged. The abdomen was flat, and a round, irregular, indefinite swelling in the right inguinal region was thought to be the distended colon. No pelvic or rectal examination was made.

Operations. A radical operation for the removal of the tumor in the right breast was performed, 14

days after which the abdomen was noted to be considerably enlarged by irregular, semi-elastic and tender tumors in both sides of the lower abdomen. An abdominal operation showed two multilocular tumors on either side of the uterus, involving both tubes and ovaries, and extending to the bladder wall, and, superficially, to the uterine wall, which was removed. The patient died 14 days after the second operation.

Autopsy. In the upper angle of the wound that was made for the removal of the right breast were two small masses. In the left breast was a rather flattened tumor, measuring 8 cm. in diameter. With the exception of adhesions between the lungs and diaphragm, the thoracic cavity appeared to be normal. In the lower third of the scar in the abdominal wall were small, ulcerated areas. The peritoneum appeared to be enormously thickened, white, and opaque. Old and recent adhesions were universally present, and the peritoneal cavity filled with clear, yellow fluid. The pelvis appeared to be filled with tumor tissue. Both the pancreas and kidneys were studded with tumor masses, the former showing practically no normal tissue. The liver was of normal size and the markings were indistinct. The spleen was of normal size and of a dark color. The presence of retroperitoneal lymph-nodes was not noted.

The tumor of the right breast. The cut-section shows a peripheral layer of apparently normal breast tissue, varying in width from ½ to 2 cm. The remainder of the breast consists of a homogeneous pale yellow mass of tumor tissue, which in some places is seen to penetrate the peripheral layer of normal tissue. The *histological structure* of the *mammary tumor* consists of a diffuse mass of small or moderately sized round cells with deeply stained nuclei throughout the entire growth. There is little stroma to be seen and the signs of an alveolar arrangement are indistinct. There are scattered about in some areas fragments of a connective-tissue reticulum, and a fibrillary stroma can be seen now and then between apparent groups of cells, but, for the most part, whatever suggestion there is of an alveolar formation is outlined by the grouping of the cells rather than by the arrangement of the stroma.

The ovarian tumors. The ovaries are converted into two large tumors, of which the smaller one, of the left ovary, measures 10 x 5 cm., and presents externally the normal ovarian shape. Its cut-surface shows a pale yellow, homogeneous surface. The larger tumor, of the right ovary, measures 14 x 8 cm., and is distinctly divided into large and small lobes which are grouped about a common center. The cut-surfaces are less homogeneous than those of the left tumor, and are traversed by numerous white trabeculae. The cortical area in both tumors appears to be thickened. *The histology* of the *ovarian tumors.* There are no traces of normal ovarian parenchyma. The tumors show a diffuse growth of small or moderately sized round cells, similar to those in the mammary tumor. Throughout a large part of the growths there is little stroma to be seen, but as the peripheral area is approached more stroma appears, inclosing a few cells in such a way as to suggest an alveolar formation. Upon the external edge of the peripheral layer there is a quite distinct alveolar arrangement (Fig. 1). The cells, however, are often grouped together in the center, leaving an irregular space between the cells and the surrounding stroma. Where the stroma is loosely constructed, one, two, or three cells are seen within the stroma meshes. Numerous places show a long double row of cells enclosed within a fine, almost fibrillary connective tissue. There are a few small vessels containing a little blood, and other small, perhaps lymphatic paths.

The metastases in other organs. The uterus, which is slightly enlarged, shows an infiltration of its outer musculature with the same type of cells as those described in the mammary and ovarian tumors. The small portions of the broad ligaments that are attached to the uterus and the mesosalpinx of the right tube, are thickened by the tumor invasion. The colon shows no ulceration or involvement of the mucosa, but its outer walls are uniformly thickened, presenting the same pale yellow, homogeneous appearance that the tumor tissue does in the other organs. The kidneys, spleen, and the liver also, show a similar peripheral tumor infiltration: it is especially marked in the kidneys.

We have to regard then in this case a very malignant and rapidly growing tumor, the histogenesis of which does not admit of a perfectly definite interpretation. The causal relations between the mammary and ovarian tumors are definitely certain, but the determination of the primary site is difficult. The writer has been unable to find a similar case in the literature, and secondary invasion of the breasts from tumors in distantly located organs appears to be rare. From the clinical history of this case it is also difficult to decide. The tumor of the right breast evidently controlled the clinical picture before the first operation and during the following ten or more days. No pelvic examination was made during this period, but from the abdominal examination made before the first operation it seems reasonable to suppose that the tumor of the right ovary, at least, already was present when the mammary operation was performed. The occurrence of the miscarriage two months before the mammary tumor was first noted also suggests the presence of a pelvic tumor at this time. The gross pathology of the mammary tumors suggests their

secondary nature. The histology of both the ovarian and mammary tumors admits of two interpretations. They may well be diagnosticated as lymphosarcomata, but the structure of the ovarian tumors points to an epithelial origin, from which has arisen an indifferent and rapidly malignant cellular growth. The alveolar-like appearance in the peripheral areas of the ovarian tumors suggests (Fig. 1) the preservation, to a slight degree, at least, of the original type of tumor in its primary site. The route of metastasis in this case is also difficult to determine, but the absence of metastases in the thoracic viscera is suggestive, in the light of Handley's observations, of a peritoneal invasion through the abdominal wall. Upon the peritoneal surfaces no nodes of implantation were noted, but the peritoneal surfaces show a white, opaque thickening surrounding all the organs, from which, as in the liver, spleen, kidneys and uterus, are numerous irregularly shaped invasions of the tumor-cells into the parenchyma of these organs. While differences of opinion in regard to the pathogenesis of this case are certainly admissible, the writer, at the suggestion of Professor Ewing, has designated the condition as a rapidly growing, embryonal type of carcinoma, in which the primary site was probably in the right ovary.

CASE 2. Recurrent carcinoma of the breast. Metastasis in the ovary by retrograde transportation through the retroperitoneal lymph-nodes.

Clinical history. A single woman, 36 years of age, noted two months after an operation for carcinoma of the left breast, and six months prior to her admission to the hospital, a swelling above the left clavicle and in the left axilla. Four weeks prior to admission nodes appeared in the right side of the neck, and the masses in the left neck and axilla had grown to a large size.

The autopsy. In addition to large masses above both clavicles and in the left axilla, numerous nodes were present over the anterior chest wall, in the epigastric triangle, and over the abdominal wall, extending down to Poupart's ligament. Both pleural cavities contained bloody serum. The lungs were not involved, but large nodes filled the mediastinum, extending to the diaphragm. In the abdomen there were nodes in the portal fissure, in the spleen, along the splenic artery, throughout the mesentery, and retroperitoneal lymph-nodes, extending from the diaphragm down and into the pelvis. There was a large node in the right broad ligament. The omentum contained no metastases, and the peritoneum showed no disseminated nodes of implantation. There was one subperitoneal node upon the small intestine. The uterus and left ovary were normal.

The right ovary is of nearly normal size. Its cut-surface shows a round white node which includes about one-half of its area. The histological structure of this node is that of a large alveolar carcinoma, extremely cellular and sharply defined from the other part of the ovarian structure, which shows numerous corpora fibrosa and the structure of a fairly atrophic normal ovary. No cancerous areas can be found outside the one node, even in the hilum or mesosalpinx. The structure of the cancerous node is exactly the same as that of the other abdominal metastases.

Metastasis undoubtedly occurred in this case by retrograde transportation through the extraperitoneal lymph-nodes, either by a direct extension through the posterior attachments of the diaphragm from the mediastinal lymph-nodes, or by a lymphatic extension from the nodes in the portal fissure of the liver, which became involved by a permeation of the lymphatics of the abdominal wall. Peritoneal implantation can be reasonably excluded.

Cases 3, 4, 5, and 6 were recurrent carcinomata of the breast in which there were negative findings in ovaries removed by operation.

The literature includes so many references to the possibility of the frequency of ovarian metastases in cases of primary cancer of the breast that the writer will merely report negative findings in four cases in which the Beatson operation was performed at the General Memorial Hospital, as an additional therapeutic resource to the use of the X-ray, in cases in which otherwise the prognosis seemed, undoubtedly, to be hopeless. In each instance a radical operation for the removal of the primary mammary tumor had been done. No definite conclusions, of course, are possible from a consideration of the histology of so few ovaries.

In Cases 3 and 5 the fibrosis of the cortical areas, which is consequent upon the slow resolution of the corpora lutea during the latter part of the ovary's functional activity, is so extensive as to appear to preclude the invasion of cancer-cells from implantation upon their surfaces. Indentations of the germinal epithelium by reason of the atrophic changes, in some places almost reaching the medullary area, suggest themselves as favorable sites for

the implantation of cancer-cells, but, in both cases, we find in the vascular zone such advanced changes in the vessel walls — not infrequently to the extent of almost complete obliteration of the vessel lumen — that an unfavorable soil would appear to be furnished for the growth of tumor-cells, whether they gained access to the ovarian structure through these fissures, or through the lymphatics of the hilum. In Case 4 the dipping of the germinal epithelium into deep crevices is most marked, and there are numerous signs of more recent functional activity than in the ovaries of the other cases. Corpora fibrosa are to be seen less advanced, and in one ovary there is a large corpus luteum, showing only moderately advanced regression changes. A follicular cyst is also to be seen, lined by one layer of columnar epithelium, which projects upon the ovarian surface, being covered only by a thin fibrous layer. In the medullary zone also the blood-vessels do not show the same changes in their walls as in Cases 3 and 5, so that the invasion and growth of tumor-cells would appear to be quite possible. In Case 6 the fibrosis is well marked but the cortical surface is not convoluted as in Cases 3 and 5, and the germinal epithelium, which is well preserved in numerous places, does not dip into the ovarian stroma. There are also several follicular cysts. The changes in the vessel walls of the medullary zone are only moderately advanced.

Case 7. Large bilateral "Krukenberg tumor" of the ovaries. Probably secondary to a gastric or intestinal growth.

Clinical history. A single woman, 28 years of age, had suffered for a long time from constipation, digestive and intestinal disturbances, which had become markedly worse during the three months prior to her admission to the hospital. She had been treated by gastric lavage by several physicians. Abdominal distention and pain in the lower abdomen had been recently especially severe. The operation for the removal of the tumors was difficult because of the presence of adhesions, but no gastro-intestinal lesion was noted. Vomiting and abdominal pains were the special clinical features until just before death, which occurred eight weeks after the operation, when intestinal hæmorrhages were also noted. No autopsy was performed.

Gross pathology. Both tumors are large; the larger one, of the right ovary, measuring 12 x 15 x 5 cm., the smaller, 8 x 11 x 5 cm. The normal ovarian shape is in general preserved, but their external surfaces are bossed, particularly that of the smaller tumor, which suggests a bilobed structure. The cut-surface of both tumors shows a solid structure, but not of an homogeneous consistency. There is a firm, thin capsule, within which numerous dense, but comparatively thin, trabeculæ traverse the tumors in different directions, dividing the surfaces up into soft, pale yellow, or white, rather homogeneous areas of tumor tissue. In places where the tissue is soft and the spaces have more or less of a circular outline, there is a honey-combed appearance. Small cysts are present, especially beneath the capsule: in the larger tumor there is a larger hæmorrhagic cyst, and near are dark areas, evidently the result of blood extravasations.

Histology. There are no normal ovarian structures. The capsule consists of a thin, dense connective-tissue layer, in and immediately beneath which are cysts, containing no epithelial lining: some are filled with blood. The structure of both tumors appears to be fairly uniform, consisting of a fine fibrillary stroma, interlacing in all possible directions, and inclosing tumor-cells of different number, size, appearance and arrangement. Depending upon the stage of mucoid degeneration which the tumor-cells have reached, they appear as round, small, with a well-stained nucleus, or as moderately swollen, with a slightly transparent cell protoplasm and a nucleus pushed slightly to the side of the cell body; or, in the advanced stages, a large, swollen, and clearly transparent cell-body is seen, with a nucleus pushed to the edge of the cell in the shape of a seal-ring (Fig. 2). In areas where the cells are few and the degenerative changes are marked the structure has a distinctly myxomatous appearance (Fig. 3). In other areas, as along the inner border of the capsular layer, where the connective tissue is denser, one, two, or three large epithelial-like cells may be seen in a single row between the stroma fibrils. Between these extreme arrangements, the cells are variously grouped within the meshes of the stroma, often showing a moderately distinct alveolar form (Fig. 4). In general, the alveolar arrangement is indistinct, but the cells are apparently of epithelial origin and are distinctly separated from the connective-tissue cells, which, in this case, are sparse even in the parts where the connective tissue is abundant. In some areas near the larger trabeculæ, the appearance is similar to that of a scirrhous growth. In sections stained with thio-saffronin, the epithelial nature of the cells, as distinct from those of the stroma, is easily distinguished.

Without the evidence that an autopsy would furnish it is impossible to state definitely that the ovarian tumors in this case were secondary to some tumor of the gastro-intestinal tract, but the clinical course of the disease, both before and after the operation, is suggestive that such a growth of a primary nature may have existed.

Case 8. Histological sections of a "Krukenberg tumor."

With the naked eye the sections appear to include the greater part of an ovary enlarged to twice the normal size. The tumor growth apparently involves the entire ovarian structure, with the exception of a narrow zone of the cortical area. In places it penetrates this area to the ovarian surface, there being only a very thin layer of fibrous connective tissue on the surface.

The histology of this tumor presents the same general structure as that of the preceding case. The stroma, however, is in greater abundance and has more of a cellular character, while the tumor-cells within its meshes are decidedly fewer. It is difficult to detect more than two or three of such cells grouped together. Throughout the section the outlines of the cell body are either indistinct, or they have been entirely destroyed by the mucoid degeneration so that there are often only the remains of a few scattered nuclei, making it difficult to differentiate the epithelial-like cells from those of the stroma.

CASE 9. Primary diffuse carcinoma of the stomach. Metastatic Krukenberg tumor of the ovary.

Only the sections for histological examination are available to the writer, which include a section of a diffusely infiltrating scirrhus of the stomach, a section of the mesentery and of both ovaries.

The tumor of the stomach shows a diffuse fibrous carcinoma penetrating all of the coats of the stomach wall. The section of the mesentery shows the typical structure of a Krukenberg tumor, having more of a connective-tissue stroma than the writer's Case 7, but the epithelial character of the tumor cells is more easily distinguished than in the writer's Case 8.

An apparently normal sized ovary shows about two-thirds of its area to be that of normal atrophic structure. Two follicular cysts and numerous corpora fibrosa are present. The stroma does not show an abnormal cellular infiltration. Adjoining the normal area, but sharply defined, there is a nodular growth of tumor tissue, which is similar to most of the structure in the writer's Case 7, except, perhaps, the cells are less numerous. In the middle of this growth is a small normal epithelial structure, having the appearance of a graafian follicle. The tumor-cells are exactly the same as those in the growth in the mesentery, both tumors being undoubtedly secondary to the growth in the stomach.

CASE 10. Primary diffuse carcinoma of the stomach. Metastatic carcinoma in atrophic ovaries. Peritoneal implantation.

The stomach, portions of the intestine and mesentery, the uterus, ovaries and tubes, with a part of the broad ligaments, vesico-uterine and recto-uterine folds, removed at the autopsy of a woman, 65 years of age, show the following conditions: The walls of the stomach are converted throughout their entire extent into a thick, dense wall of tumor tissue. Similarly, but less so, the mesentery and intestinal wall is thickened, and over the peritoneal surfaces are scattered very small and slightly elevated nodules. The peritoneal surface of the pouch of Douglas and the vesico-uterine folds are studied with similar nodules. The uterus is small, and both ovaries are markedly atrophic, having a long spindle shape.

Histology. All of the layers of the stomach wall are infiltrated with a diffuse carcinoma, showing in numerous areas the structure of a fibrocarcinoma. In the intestinal wall the growth is limited to the peritoneum and subperitoneal tissue, completely surrounding the muscularis except at the mesenteric border, where the growth follows the peritoneal layers of the mesentery, between which is a space of normal fatty tissue. A section through the bottom of the pouch of Douglas shows the same type of growth which is limited to the peritoneal and subperitoneal layers. It gives the general appearance of a fibrous thickening of the peritoneum that is infiltrated with cancer-cells. No cancerous changes are found in the tubes or uterus.

Both ovaries, which are in an advanced stage of fibrosis, show areas of early cancerous invasion which undoubtedly represent the implantation of metastatic cancer-cells from the growth in the stomach. They are more advanced in the left ovary. The germinal epithelium is preserved in a few places, but in several places over the cortical zone there is a covering of tumor growth, of varying width, of the same histological structure as the growths in the stomach, intestine, and pouch of Douglas (Fig. 5). In some places it is very thin, only one, two, or three rows of epithelial cells lying within a fibrillary stroma; while in other places it widens out, invading irregularly the fibrous stroma, but not infiltrating deeply the cortical zone, except in one area near the inner pole of the left ovary. A section which was made at the junction of the left uterine ligament with the ovary shows two breaks, apparently, in the peritoneal covering, by more or less wedge-shaped invasions of tumor cells, beneath which are two or more small, round, isolated foci on the border between the cortical and medullary zones. There is also in the right ovary a similar small, deeply located focus near the junction of the cortex and the hilum. In the areas immediately adjoining the cancerous invasions there is no evidence of a reaction of the ovarian stroma in the form of cellular hyperplasia, but there does appear to be considerable œdematous infiltration, by reason of which the stroma is more loosely constructed, showing in a few places the suggestion of a myxomatous structure. Some of the cells in the ovarian metastases, as well as those of the other metastases and the primary growth in the stomach, are slightly vacuolated, and show considerable swelling of the protoplasm from a mucoid degeneration, so that the nuclei are slightly pushed to the sides of the cell body, but the degenerative changes are not uniformly present and have not anywhere reached the extreme stage that is so often noted in these tumors.

SUMMARY

The writer, from this review of the literature and his own personal observations, feels justified in directing attention to the following points regarding the subject of metastatic carcinoma of the ovary:

1. Malignant tumors of the ovaries, even when of such size as to control the clinical

course of the disease, are frequently enough secondary to growths in other organs, especially the stomach and the breast, as always to justify a suspicion of their secondary nature, before any method of treatment is advised, or a probable prognosis is defined.

2. The possibility of metastatic invasion of these organs should always confront the surgeon in dealing with the problem of treatment and prognosis in cases of primary growths in the stomach and breast. This is especially so in cases of recurrences in the chest wall, or in the other breast, after operations for the removal of the primary mammary tumor have been performed.

3. The route of metastasis is rarely a chance distribution by embolic transportation through the blood or lymphatic vessels, but occurs, either by a direct extension through the retroperitoneal lymph-nodes by permeation or retrograde transportation, or by peritoneal implantation.

4. Peritoneal implantation is undoubtedly a more frequent route than has previously been supposed; and next to the liver, the ovaries, especially during the period of their functional activity, are more often involved in this way than any of the other intraperitoneal organs, because of their circulatory changes, the traumatism of their surface from ovulation, and the proximity to the pouch of Douglas, which is apparently more frequently the site of peritoneal implantation of cancer-cells than any of the other peritoneal surfaces.

5. The gross appearance of the ovarian tumors, when they are large and extensively involved, is not characteristic, but in the earlier stages, secondary invasions usually appear as distinct nodes, located in any area, and involving a small or a large part of the ovarian structure.

6. The histology of these tumors varies with the nature and location of the primary growth, but their morphology is undoubtedly often altered by the changed conditions of nutrition and growth which the ovarian structure offers. The adenocarcinomatous type appears to be frequent, but a larger number are of the diffuse infiltrating type, in which the glandular structure is lost, often showing a distinctly fibrocarcinomatous structure similar to the structure of the primary tumor in the stomach or breast from which they are derived.

7. The Krukenberg tumor may be a primary growth, but in the vast majority of cases it presents the histology of a secondary, diffuse, infiltrating carcinoma, which derives its features from those of a primary growth in the stomach, or from degenerative changes which are so common to all forms of ovarian growth — myxomatous degeneration, mucoid degeneration of the cells — and, frequently, from a reaction of the stroma to the invasion of cancer-cells in the form of a cellular hyperplasia.

The writer desires to express his appreciation of the numerous suggestions and criticisms which Professor Ewing has offered in the course of this study. He also desires to thank Dr. Elser and Dr. L'Esperance for much of the pathological material, and Drs. Lee and Hitzrot, of the New York Hospital, and Dr. Mallett and the House Staff of the General Memorial Hospital, for access to the clinical notes of the cases.

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ANTERIOR TRANSPERITONEAL HYSTEROTOMY[1]

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IN surgical diseases it has been proved by modern surgical methods that the best way to attack a pathological condition or unfold a puzzling symptom-complex is to expose the afflicted parts to the light of day and to the eye of the surgeon. By so doing a fuller comprehension of the living pathology present may be gained, the greatest relief obtained with the least sacrifice of function and tissue, and a guarantee against future complications afforded.

One by one the cavities of the body have yielded to the surgeon. The treatment of hidden surgical diseases has improved in direct ratio with the boldness of exposure and directness of attack. We are sure that uterine disease also will be better treated when many of the present blind methods of diagnosis and treatment have given way to direct inspection and treatment under the guidance of the eye.

In advocating the operation of hysterotomy I bear in mind the fact that I have been doing it for years with no mortality and with the satisfaction of knowing that certain obscure conditions have been found and eliminated by early and radical means, which, by the more conservative methods now in vogue would have failed both of early diagnosis and proper treatment. I firmly believe that the early diagnosis and cure of malignant changes of the fundus can be made best by hysterotomy and that the large maternal mortality in placenta prævia can be reduced almost to nothing by this operation, while the fœtal mortality will be greatly improved. In addition to these clean-cut indications for hysterotomy the procedure will be found most useful in clearing up the exact condition in many cases now beyond our diagnostic powers, and in this way the seemingly radical proposal will result in the most conservative surgery adapted to the individual case.

The operation is not new in the history of medicine, having been performed many times in the past, but at first, only as a terminal procedure on dead or dying mothers in the hope of obtaining a living child. Later it was used in the attempt to save both mother and child after many vain attempts to deliver *per vaginam*, and, lacking the modern safeguard of asepsis, produced a frightful mortality.

Hysterotomy prior to the seventeenth century has no practical interest although the first recorded case in which the operation was done on a living woman was in 1500 by Jacob Unfeil, a butcher, who saved his wife and later is reported to have operated on several other women with success. In 1610 the well authenticated case of hysterotomy by Trautman in Germany is recorded; but up to 1893 only 37 to 40 per cent resulted in recovery.

Blensdell, in 1834, reported 23 cases, the only ones in England before 1821, all of whom died except one. For a period of twenty years in Paris there was not a single recovery from this operation. From 1891 to 1896 the mortality was 38 per cent; in 1902, 20 per cent; and it was further reduced in 1904 to 12 per cent.

The operation of hysterotomy or cæsarian section has always been saved as a last resort, and the crude efforts of our ancestors to avoid the peritoneum in its performance explain this great mortality.

The operation until recently has been exclusively in the hands of the obstetricians, and only obstetrical conditions have justified in their minds its performance, but obstetrics is notably conservative, as was gynecology until a few years ago. While natural methods are always preferable, it must be granted that in the presence of pathological conditions it is not wise to rely upon them until the patient has been exhausted or her tissues torn and lacerated by methods directed from below, with the result that when hysterotomy is finally done life is sacrificed by watchful waiting and the mortality advances to the point that condemns the procedure.

Especially does this obtain in placenta

[1] Read before the Springfield Academy of Medicine, Springfield, Massachusetts, September 14, 1915.

prævia, for which obstetricians still claim that version is the operation of choice. In the last analysis, however, any procedure must stand or fall upon its mortality and unless the obstetrician can show that his methods are equal or superior in their results to hysterotomy he must yield.

It is conceded by everyone that certain degrees of contraction of the pelvis are indications for hysterotomy, but I believe and advocate its performance in placenta prævia, premature separation of the placenta, severe toxæmia of pregnancy and eclampsia, in some cases of pyelitis of pregnancy with marked septic symptoms, in certain cases of submucous fibroids, in cases of unexplained uterine bleeding in middle aged females at or near the cancerous age, and in cases of prolapse of the cord with a living child and a rigid and non-dilatable cervix.

In advocating such a wide performance of this operation I suggest that certain rules of technique be followed:

1. Rigid asepsis.
2. Careful delivery and walling-off of the uterus from the general peritoneal cavity.
3. Early operation before manipulation from below has sapped the patient's strength and introduced infection.
4. Careful closing of the uterine wall.

The operation is simple, easily carried out, relatively free from risk, obviates vaginal or perineal lacerations, and recovery is rapid. There is, in cases at term, no pain of prolonged labor and the fœtal mortality is low.

In the past five years I have performed hysterotomy in 64 cases. The general indications for its performance have remained as stated by me in my last paper in June, 1914: (1) to establish a prompt and certain diagnosis when a reasonable suspicion exists of malignant disease of the interior of the uterus; (2) to terminate pregnancy promptly in cases in which life is acutely endangered by the continuance of that condition.

The pathological conditions found were as follows:

Simple myoma of pregnant uterus	3
Symmetrical myomatous enlargement of uterus	8
Retained products of conception causing suspicion of malignant disease	10
Premature separation of placenta, suspected of placenta prævia	10
Chorio-epithelioma	1
Early carcinoma of fundus	1
Chronic hyperplastic endometritis	6
Benign polyp of the endometrium	3
Contracted pelvis (fœtus at term)	1
Toxæmia of pregnancy	3
Toxæmia of pregnancy and eclampsia	2
Placenta prævia	10
Septic pyelitis	5
Dead fœtus in tuberculous mother	1
	64

There was no maternal mortality in the pregnant cases. Three children lived, the remainder all being under six months and non-viable. The average stay in the hospital of all cases was 19.7 days, and convalescence was uneventful; only 2 had post-operative pain, 4 bled slightly from the cervix, 29 had no pain the first night, and 2 had slight skin infections.

The average number of children born to these patients was 4. Miscarriages and previous difficult labors were found sporadically in the series, but had no statistical value.

Except for those outspoken cases of pregnancy in which the operation was dictated by the necessity of prompt and thorough evacuation of the uterus, these cases were characterized chiefly by the lack of symptoms that would enable a diagnosis to be made by any other means than that employed.

Those cases of pregnancy accompanied by pathological lesions had a duration of only 3.9 months, and as the lesion was sufficient to have caused risk of life to the mother termination at this time was justifiable.

Of the above cases, placenta prævia seems to invite most discussion as to the propriety of doing hysterotomy or version. McDonald, reporting the results in 8,625 cases, shows a maternal mortality in all cases of 7.22 per cent and a fœtal mortality of 55 per cent; in central placenta prævia a maternal mortality of 15 per cent and a fœtal mortality of 71 per cent; and in marginal placenta prævia a maternal mortality of 4.8 per cent and a fœtal death-rate of 58 per cent.

The great danger following a natural delivery in placenta prævia is the post-partum hæmorrhage, occurring as it does in a patient already sadly depleted by bleeding. Those who have delivered cases by the abdominal

method are impressed with the great control of hæmorrhage by the operator and its immediate cessation in comparison to the vaginal method.

I have 10 cases in this series of placenta prævia on which a hysterotomy was done. The maternal mortality was nil, the fœtal mortality was 43 per cent, due to the fact that cases were usually bleeding profusely when admitted to the hospital and were in the early stages of pregnancy before a viable child could be delivered and survive. The average length of the duration of pregnancy at the time of operation was 4.7 months, the longest being 8.5 and the shortest 3 months; one at full term done nine years ago has a perfectly healthy child now living. The average number of days spent in the hospital was 17; longest 28 days and the shortest 11 days.

All cases had uneventful recoveries, none having post-operative pain or fever.

Eclampsia, another indication to my mind for hysterotomy, is an auto-intoxication owing its origin to the pregnant state, and, although we must admit ignorance of its true etiology, we do know that throughout the course of the disease there is a profound disturbance of metabolism. There is no specific therapy, and the only rational cure for this intoxication is to remove the cause. Palliative measures should be used at first, but they should not be carried to the point of exhausting the patient or allowing her to become a poor surgical risk by the weakening effect of frequent convulsions.

According to Peterson the mortality of eclampsia increases with the number of convulsions and manipulations from below preceding operation.

Number of Convulsions	Cases	Deaths	Mortality per cent
1 to 5	237	44	18.5
6 to 10	129	26	20.1
11 to 15	37	10	27
16 to 20	16	6	37.5
21 to 23	8	4	50
26 to 40	6	5	83.3
60 to 64	2	2	100

Lupman reports from the clinics of Wurtzburg, Basel, Halle, and Berlin a mortality of 23 to 30 per cent, by expectant treatment, and 2.8 per cent or even 1.8 per cent after immediate operative delivery. Zweifel reports an expectant mortality of 28.5, operative 11.25 per cent. Baum and Ferie of Milan report an expectant mortality of 30 per cent with an operative mortality of 2.3 per cent and 7 per cent respectively. Peterson, out of 290 cases spontaneously delivered, reports a maternal mortality of 18.96 per cent and an operative mortality of 14.96 per cent. The German statistics show an expectant mortality in 390 cases of 28.9 per cent, and an operative mortality in 615 cases of 15.9 per cent. Kroenig and Sellheim have 26 cases, all mothers and children recovering after this operation.

While such figures do not mean that every woman with antepartum symptoms of eclampsia should be subjected to the operation of hysterotomy, they do mean that we should revise our opinion regarding the status of this operation when indicated.

Manual and instrumental dilatation of the cervix is attended with grave immediate and remote dangers; it aggravates the eclamptic seizures causing shock and deep cervical tears, hæmorrhage, and infection, while in hysterotomy you have a clean-cut tissue rather than a divulsed one, less shock, less danger of infection, and at all times you are master of the situation.

One of the abnormalities of childbirth producing a large maternal and fœtal mortality, is premature separation of the placenta with concealed or accidental hæmorrhage. Everyone has met with cases of this dangerous complication of labor when an inert uterus is distended with blood complicated by a further post-partum hæmorrhage after delivery. These cases must, of course, be packed, which gives rise to infection in a large percentage of cases. When the uterus is tense and tender and cannot be made to contract and the concealed hæmorrhage is increasing, the patient becoming more collapsed, abdominal hysterotomy is indicated because it is quickly performed and hæmorrhage, if it occurs, is under the eye. There were 10 cases of this complication in our series. The average stay in the hospital,

was sixteen days; all the mothers recovered and left the hospital in good condition.

In 7 cases an hysterotomy and appendectomy were performed; in three, simple hysterotomy.

The symptoms complained of were variable; 5 had pain in the lower abdomen, 1 in the back, and 2 had no pain at all.

Hæmorrhage was severe in 6 and slight in 3 cases, the duration of the hæmorrhage averaging seven weeks. The menstrual history was not conclusive. Seven had borne children, 2 were primiparæ. The abdominal examination showed nothing but tenderness in the lower quadrants and about McBurney's point. The vaginal examination showed vaginal bleeding in only 2 cases.

The operative findings showed degenerated placenta in 5 cases, partially separated placentas in 4, and entirely separated in 3 cases. The fœtus were all dead, the course of pregnancy having continued for an average of only four months and but 1 being over five months. All recovered, 1 was slightly shocked after operation and 2 had a slight wound infection.

In 5 cases hysterotomy was done because of severe renal infection during pregnancy, amounting almost to sepsis.

Simple pyelitis is not an indication for hysterotomy, local and medical palliative methods should first be tried in all cases and usually will affect a cure; but when, after having tried the above, the septic condition increases, evacuation of the uterus by the transperitoneal route is advised. When patients are able to command facilities for medical treatment they should be allowed to continue to term if possible, but in hospital practice this is not always possible. A parturient woman with an active infective process is in great danger of post-puerperal sepsis and the life of the mother in this class of cases is the paramount consideration. It must be emphasized that renal infection *per se* in the pregnant woman is not an indication for this operation, which must be reserved for those desperate cases in which prompt action is needed to save life.

The operation performed in these cases was simple hysterotomy and delivery in 3 cases; hysterotomy, delivery, and appendectomy in 2. The average stay in the hospital was sixteen days, all mothers recovering and leaving in much better condition than on entry.

Twenty-one cases were operated on because of bleeding which aroused suspicion of malignant disease of the interior of the uterus. Ten of these cases showed retained products of conception. I would naturally wish to avoid hysterotomy in these cases but the circumstances were such that pregnancy did not seem a probable explanation of the symptoms. Such errors are possible under this method of procedure, but in extenuation it may be said that not one received any apparent harm from the operation and departed cured. Of the remaining cases there were 5 that in my mind, justified the procedure, since malignant disease was discovered in 2 and benign polyp of the endometrium in 3. One case showed an early chorio-epithelioma and has remained well since hysterectomy. Another showed a very early carcinoma of the left cornu and likewise has remained well after removal. The 3 cases of polyp were readily rid of this pathological condition without removing the uterus. These cases were particularly satisfying as it has happened to me on a number of occasions to fail to remove such polyp by scraping, causing a diagnosis of essential hæmorrhage or malignancy with summary removal of the uterus only to find a simple condition easily remediable by hysterotomy.

The majority of these cases had been curetted one or more times without relief prior to the operation. I do not advocate hysterotomy when one curettage has afforded some relief; but the inadequancy of the curette is demonstrated on opening the uterus after its use and the histories of many patients are the histories of many such scrapings with no relief.

Blind scraping of the inside through the cervix with a sharp curette is one of the most pernicious practices in medicine. It is done on the slightest excuse, and the result is that the endometrium, glands, and all functionating tissue are removed with no relief of the trouble, and often there result in addition menstrual disturbance and sterility. Those

cases in which the uterus was opened and no further pathology found than a chronic hypertrophic endometritis were curetted through the opening in full sight, which could be done gently and effectively.

In 2 cases myoma was found complicating pregnancy, the fœtus was sacrificed, the myoma removed, but the uterus was saved for future pregnancies.

Another type of myoma in which hysterotomy is of value is that which produces a symmetrical enlargement of the uterus indistinguishable to sight and touch from normal pregnancy. I can agree with Maurice Richardson when he said that he could not always tell a pregnant uterus when he had it in his hand. Every operator of experience has met with cases presumably of tumor in which after opening the abdomen he is disconcerted by the great resemblance to pregnancy. I have closed the abdomen in such cases only to be compelled to operate after an interval had proved that the condition was really tumor and not pregnancy. In eight cases I have applied the crucial test of incision rather than risk removal of a uterus which was possibly pregnant and in all verified the diagnosis of myoma before proceeding further.

These classes of cases are the ones that involve difficult problems of diagnosis and treatment and have led me to advocate this operation. I acknowledge that at times conditions are found which could be relieved from below, but the lack of danger in performance of this operation, the satisfaction of seeing your field and exploring it thoroughly before closing, and of being able to find or eliminate early carcinoma with reasonable certainty, outweigh all arguments of excessive surgery.

There is no danger in future pregnancies if you cut well and sew well using absorbable sutures and putting the sutures down to, but not through, the endometrium. In experiments on guinea pigs carried on at the Lying-in Hospital in New York, it was found that, after opening and carefully suturing the uterus, the scar was very difficult to find on microscopic examination.

When non-absorbable sutures are used, or when the uterine incision becomes infected a stretching of the scar sometimes results, but there are only 26 cases on record out of the many hysterotomies done in which a uterine scar has ruptured in a subsequent pregnancy.

The operation of extraperitoneal hysterotomy has gained wide popularity with some operators. It was revived in 1906 by Frank, having been attempted in the earlier days of abdominal surgery when asepsis was unknown, in the effort to avoid opening the general abdominal cavity.

The operation is a suprasymphyseal section of the lower uterine segment under the anterior reduplication of peritoneum. There are in all sixteen techniques with a 6 per cent maternal mortality.

The method now used is not strictly an extraperitoneal section as the peritoneum is opened. It is performed in the following manner; a paramedian, median, or Pfannenstiel incision is made though skin and fascia, the parietal peritoneum is exposed and opened in a straight line parallel to the long axis of the body, the uterine reduplication of peritoneum is also opened and either sutured or clamped to the cut edges of the parietal layer, the uterus is opened and the child delivered, and the peritoneum is now resutured to its original layer.

This operation was vaunted in infected cases, but having proved a failure in these was advocated in clean cases as more efficient than the classical method.

The objections to this procedure are many. In the first place stitching the peritoneum in virulently infected cases does not make it germ-proof, for the peritoneum after being separated laterally from the uterus is lacerated and lowered in vitality and is more quickly infected; there is, especially in early labor, insufficient space for the uterine incision; there is danger of bladder injury and the head must be pried out of the uterus or dragged out with forceps which is more likely to cause injury or death of the child. It is admitted by its advocates to be a much more difficult and dangerous operation than the classical one and has no special advantages.

The vaginal method of hysterotomy is used extensively abroad and is only applicable

in obstetrical conditions and even then has many drawbacks. It is more difficult to perform, there is always a danger of injuring the bladder, the cervix is hard to draw down, there is difficulty in suturing accurately in a narrow pelvis, and there is a very poor exposure of the interior of the uterus.

Finally, I claim the operation of anterior transperitoneal hysterotomy is a most valuable addition to the general surgeon in the course of his pelvic work; it gives him a method of making a diagnosis in early malignancy and saving life in many dangerous complications of pregnancy. It is easy, simple, and safe. Its success depends on the early recognition of the necessity of doing it.

THE ROENTGEN TREATMENT OF UTERINE CARCINOMA[1]

By JAMES T. CASE, M.D., F.A.C.S., Battle Creek, Michigan

IT has been suggested that in this evening's discussion you will be more interested in a practical summary of the roentgen treatment of uterine carcinoma, dealing with results and present technique, than in a dissertation upon the histological, theoretical, and experimental data upon which our present knowledge of the subject is based. Assuming that you will all agree with me that purely superficial cervical epithelioma responds successfully to properly applied roentgentherapy, I will confine my remarks to an inquiry into the value of present-day deep roentgentherapy in uterine cancer which has advanced beyond the stage of the superficial epithelioma.

It needed but a short while after Roentgen's discovery to develop a technique for the successful treatment of superficial cancer by means of the X-rays, but nearly ten years elapsed before means were found for filtering out the softer and less penetrating rays which are active in producing roentgen dermatitis. The earlier experiments seemed to indicate that the X-rays were not satisfactory in the treatment of deeply seated lesions, but the introduction of some newer methods to be described shortly brought about a reversal of the opinion founded on the first results.

There have been a number of new developments in roentgenology, both in the production of more powerful apparatus and in the refinement of therapeutic methods, making possible more accurate estimation of the dosage. Nearly two years ago Coolidge announced the invention of a new X-ray tube which has proved to be a powerful and very precise instrument. New and powerful sources of high tension current have been devised. The technique of irradiation has been much improved by the adoption of cross-fire methods and the practice of filtration. It is no longer considered necessary to place the X-ray tube at a great distance from the skin; for, inasmuch as the intensity of the X-rays varies inversely with the square of the distance of the anode from the part under fire, it is evident that when a tube is brought nearer to the skin, the time required for a certain dosage to a deep-lying structure will be proportionately diminished. The former objection to the short focus skin distance was the much greater danger of injury to the skin. Since the introduction of filtration methods, however, this danger of skin injury is eliminated to a considerable degree, and it is now possible to bring the tube much closer to the skin, thus materially shortening the time required to administer an effective dose.

These various developments have rendered possible the practical employment of effective doses of roentgen rays aggregating at least one hundred times the maximum dose considered safe ten years ago. A number of benign deep-seated affections which hitherto have responded only uncertainly to the efforts of roentgenologists now offer some of the most successful fields for deep roentgentherapy. This increasing success with benign lesions has aroused hope that by applying to malignancies the same improvements in technique

[1] Presented in the symposium on "Cancer of the Uterus," at the meeting of the Chicago Gynecological Society December 17, 1915.
(For discussion see p. 502.)

and increased dosage, we might at last find in the rays a really curative agent.

It is only proper to add the warning that this advance has been accompanied by a corresponding increase in the danger attending the unskilled application of this potent means. Hence, far greater skill and judgment is required for the successful and safe administration of deep roentgentherapy in the present understanding of the term. Not the least of the dangers involved in the present-day methods is the likelihood of giving inadequate treatment. Insufficient irradiation is likely to produce more active growth through irritation instead of the intended destruction, thus tending to render inoperable, tumors which might have been operable, and increasing the likelihood of metastasis. Without adequate filtration, the action of the X-rays, as well as that of radioactive substances, is far too intense at and in the neighborhood of the point of entrance, and far too weak a short distance away. With the recent improvements in roentgen technique, these disadvantages are, to a considerable degree, eliminated, for the roentgen tube furnishes many thousand times more rays than the available quantity of radioactive substances, and hence can be applied from a greater distance. Malignant tumors belong to a class of lesions in which treatments should be given in distinctly massive doses, and any treatment with radio-active substances which does not produce improvement is likely to cause considerable injury.

Several years were consumed in the development of these more powerful apparatus, special tubes, and improved methods. During this time numerous papers have appeared by foreign and American authors. In this country, G. E. Pfahler has taken the lead in papers dealing with the roentgen treatment of malignancies and his results seem to be the most promising. The earlier papers, which are the ones referred to in most textbooks at the present time available, dealt with cases treated by the old, inadequate methods. Hence in reaching a decision as to the present value of the roentgen method, our minds must be open to conclusions drawn from recent experimentation and the results of treatments given by the improved technique above outlined.

Attention should be called to the fact that radium- and roentgentherapy are very closely related to each other, both as to theory of effect and principles of application. In some respects it would have been more satisfactory to discuss these two subjects under one head, for certainly the most successful method of applying radiotherapy at the present time is by the combined employment of radium and roentgen rays, the radium (or mesothorium) internally and the roentgen rays externally. As will doubtless be emphasized by another speaker, in radiumtherapy we wish to utilize the γ-rays, and therefore filter out the rays of lesser penetration. In deep roentgentherapy the effort has been to utilize as hard rays as could possibly be obtained. The Coolidge tube is now available for the continuous application of hard roentgen rays with a penetration approximating that of the lower γ-rays of radium, and there is promise of still further development of its possibilities, both through increasing the penetrating power and by greatly increasing the quantity of rays which may be administered within a given time. Through the first Coolidge tubes which were kindly supplied me by Dr. Coolidge some months before they were placed upon the market, we were able to send from five to ten milliamperes of current for hours at a time at a voltage represented by an equivalent spark gap of ten inches. There is practically no limit to which the penetration of the rays from a Coolidge tube can be raised. This penetration is not measurable with the Bauer qualimeter, or with any other penetrometer now available. With the old tubes, especially when cooling with ice-water, we were usually able to reach a penetration as high as 10 Bauer and to maintain a current of four to six milliamperes continuously. The later developments in the work of Dr. Coolidge have shown the feasibility of placing at the disposal of physicians a tube backing up a parallel spark gap of fifteen inches with rays of such penetration that ten millimeters of aluminum will be required for protecting the skin instead of the three or four millimeters

now ordinarily used. In fact, such tubes are already available, with almost unlimited capacity for milliamperage (up to 100 milliamperes) and for continuous running at this great intensity.

It should further be noted that the study of histological specimens shows that there is no essential difference between the biological effects produced by the roentgen rays and by the rays of radium or mesothorium. The effects of the roentgen rays upon mouse carcinoma, as described by Contani, and independently by Wedd and Russ, agree very accurately with the histological findings after radium treatment of mouse carcinoma, as described by Apolant, Bashford, Murray and Cramer, and Wedd, Chambers and Russ. The roentgen rays brought about the same histological changes in sarcomatous growths (Clunet and Raulot-LaPointe) as were observed in a fibrosarcoma exposed to the γ-rays of radium (Dominici). In view of the fact that these conclusions have been reached independently by various observers, there is no great likelihood that the findings have been incorrectly interpreted.

Therefore the discussion of radium and roentgen rays should rightly have been included under one head, for with both agents the biological effects as well as the principles of application, including means of filtration, cross-fire, protection of patient and of operator, are practically identical. There are many who dissent from this opinion, holding that the radium or mesothorium treatment of deep-seated malignancy has a great many advantages over the roentgen method. Such opinions are probably biased, doubtless honestly, by the possession of more or less radium or mesothorium which must be made to "work." On the other hand, there are some who believe the comparison all in favor of the X-rays. Bumm in particular states from his experience of two years at the Berlin Clinic for Women that in the treatment of carcinoma, it is not possible to go deeper than two, or at the most, three centimeters with the radio-active substances without injuring the surrounding tissue. If the carcinomatous proliferations are superficial, they undergo a prompt and apparently permanent cure. But if in advanced cases, infiltration has developed in the neighborhood of the primary focus, the superficial lesions will promptly heal; nevertheless underneath the callous scar, the carcinoma will continue to grow and after six months or a year the patient will return with a cured primary focus, without secretion or hæmorrhage, but with fresh nodules grown in the deeper tissues. Attempts have been made to deepen the effect of radioactive substances by the administration of larger doses, but in a large measure unsuccessfully, because the superficial tissues situated within the zone of intense radiation suffer considerable injury in spite of all filtering, as soon as a depth of three, four, or more, centimeters has been reached. This leads to necrosis and although the patient may be clinically cured of cancer, the untoward effects from mesothorium and radium burns may lead to the patient's death. With the roentgen rays Bumm holds that they can be applied at a greater distance from the tissues and in this way the superficial layers will no longer show considerable injury, while a sufficiently strong effect is obtained in the deeper parts.

It has never been demonstrated that the effect of γ-rays on carcinomatous tissue is more intense than hard roentgen rays. In the treatment of cancer, the effect depends upon the quantity of rays absorbed by the pathological tissue, and the degree of success will improve just so far as the absorption of rays in the carcinomatous tissue can be increased. By the application of exceedingly large doses, and the use of ultrahard rays, it is now possible to obtain such brilliant results in the treatment of deep-seated tumors as have never before been hoped in the history of roentgentherapy. For the present, it must be admitted that these results are only palliative. A sufficient percentage of apparent cures lasting three or more years has not yet been obtained, so that at the present time we are not justified in claiming for the X-rays (or for radium, either, for that matter) a *curative* value.

Reference has already been made to the necessity of avoiding inadequate treatment. Experimental studies have shown that a small

amount of roentgen or radium rays has a stimulating action on tumors. One of the greatest dangers of radiotherapy, therefore, is that the dose given at the surface may destroy or injure the tissues making up the superficial layers, while the much smaller amount that reaches the deeper tissues may have only a stimulating action. Thus it is conceivable (and indeed a well-known fact) that the superficial layers of a malignant tumor may be destroyed while the growth of the deeper layers is aggravated. This effect is explained by two facts: (1) The intensity of the rays increases with the square of the distance; (2) a part of the rays are absorbed by the tissues through which they pass. Keetman's experiments show that 30 per cent of the roentgen rays are absorbed in each centimeter of tissue. Bumm claims that the destructive action of the γ-rays of radium is exhausted at three to four centimeters from the surface. As von Franqué has put it, it is not easy to steer between the Scylla of "too little" and the Charybdis of "too much."

Unfortunately the roentgen rays are not selective in the sense that they destroy only carcinomatous tissue and do not effect the normal tissue. It is true there is a certain intensity at which they can act on the different tissues tending to destroy carcinomatous cells, stimulating the growth of connective tissue around the carcinomatous tissue, and acting in a neutral manner upon other normal cells, such as epithelium. If the ray intensity is given in less than this strength, the carcinoma may even be stimulated to greater, more active proliferation. If the ray intensity is excessive, even the neighboring tissues may be destroyed. This is not only true of the roentgen ray, but also of the γ-rays of radium.

Carcinomatous tissues are quite sensitive to the X-rays. This sensitiveness, except in certain locations, is greater than the sensitiveness of the surrounding tissues. Histologically it has been demonstrated that, under ray treatment, degeneration of malignant cells may take place before any effect upon healthy cells is demonstrable. The nearer the malignant cells approach the embryonal type of tissue, the greater their radiosusceptibility; the younger pathological cells are effected by rays which have passed through healthy tissues without producing destructive changes. In comparison with other tumors, for instance lymphomata and certain sarcomata, carcinoma is less sensitive. This radiosensitiveness is, on the whole, rather moderate, varying within certain limits.

Haendly has made histopathological studies of cancer tissue of the uterus which had been subjected to irradiation. There is a primary injury of the cancer-cells which leads to a disturbance in their growth, lack of mitosis and giant-cell formation; the character of the epithelial cells is changed; and finally there is a disappearance of some of the cells through complete destruction. One notes a tendency for connective-tissue new-growth to replace the destroyed carcinoma-cells. Through overdosage, this new-formed connective tissue may become sclerotic and degenerated, just as does the rest of the connective tissue. The smooth muscle atrophies and disappears almost entirely. Some of the muscle fibers show hyaline degeneration.

The destruction of cancer-cells by roentgentherapy has been demonstrated histologically by various reliable investigators. This fact must be conceded. The histological findings reported by von Franqué in three of his own cases who underwent hysterectomy after roentgentherapy illustrate very well the different degrees of change which have been described by many authors.

The first case was a carcinoma of the cervix, just at the borderline of operability, the results here illustrating inadequate treatment. The effect of the rays was not very uniform: in some places there was no change, and in some advanced necrosis; at the boundaries between the tumor and sound tissue there were areas where there seemed to have been a stimulating action. The greater part of the carcinomatous tissue was in the stage which has been described as hypertrophic; the cancer-cells were enlarged and the nuclei plump and hyperchromatic.

The second case was an advanced typical pavement epithelial carcinoma of the cervix. The operation was performed the day after the last irradiation. The effect was much

more complete than in the first case. There were some small carcinoma nests remaining, but the great majority of the carcinoma-cells, not only on the surface, but deep in the tumor, were in varying stages of destruction. From the picture they were justified in assuming that a continuation of the irradiation would have completely destroyed the tumor. The specimen showed beautifully the different reactions of the different tissues. The epithelium of the uterine glands in the immediate neighborhood of destroyed carcinomatous foci was absolutely unchanged, while the connective tissue appeared to be undergoing active proliferation. In some places the connective tissue looked like young granulation tissue, and contained abundant multinuclear giant cells, which were doubtless engaged in the work of disposing of the dead carcinoma-cells.

The third case was a typical adenocarcinoma of the cervix, with ulceration at the os. The patient was first curetted and cauterized and then treated with radium and roentgen rays. Finally, on account of a small, persistent ulcer, the patient requested operation and the radical abdominal operation was done, a little over a month after the first of the two series of treatments which she received. The patient died six days after the operation from a cardiac complication. The outcome was all the more unfortunate because histological examination showed there was no carcinoma left after the radiotherapy. This case shows that adenocarcinoma may be cured by a combination of cautery and radiotherapy.

The effect of the radiotherapeutic treatment is very helpful in the temporary relief of symptoms. Although my remarks are intended to discourage the building up of too much hope in radiotherapy as a means of permanent cure, I would not have you discount in the least the great helpfulness of this method in a palliative way. One of the first effects of the roentgen rays is the disappearance of pain, even of severe pain, sometimes not until after a prodromal exacerbation. Even in the most unfavorable cases where the effect on the size of the tumor is only slight, quick and permanent relief from pain is often secured. Only rarely is the analgesic effect lacking. Almost all authors report at first a temporary inflammatory swelling and increased secretion from the tumor, but soon the bleeding and the putrid secretion stops and there is only an odorless serous discharge which disappears in a few weeks. With the favorable cases, there is seen within the course of a few months, or possibly sooner, a contraction of the growth; ulceration heals over, and the cervix regains its normal form. Finally senile atrophy of the genitalia supervenes. Decrease in the size of the tumor is often only superficial and unsatisfactory, but the general condition is usually improved. There is diminished cachexia and anæmia and usually the patient gains in weight.

It is regrettable that there are some untoward effects which occasionally are observed in spite of all the precautions we are at present able to exercise. As compared with the seriousness and disagreeable nature of the symptoms of carcinoma, the untoward effects are relatively unimportant. The degree to which untoward effects are experienced differs greatly according to the patient and according to the size of the doses. There may be weariness even to prostration, fever, nausea, and perhaps vomiting. If the rays are used a sufficient length of time, there may be a severe anæmia. Some of these effects are due to the rays themselves and to the changes brought about in the air in the room by the high-tension currents. Others are due to acidosis brought about by the absorption of the products of cell destruction. Bladder irritation is occasionally a distressing complication. The writer has seen rectal tenesmus in only a few cases following roentgen treatment, although after radium treatment this is a fairly common complaint. These various untoward symptoms disappear very soon after the cessation of the treatment.

Through the courtesy of one of my colleagues, Dr. Paul Roth, I have been able, in a number of cases undergoing treatment, to secure the estimation of the acidosis by the CO_2 tension in the alveolar air and acetone in the expelled air. The figures thus far have seemed to tend to support the idea advanced by S. Lange that many unpleasant

constitutional symptoms following deep roentgentherapy are the result of an acidosis, either local or general. Lange prescribes sodium bicarbonate, thirty grains every three hours, to be continued for forty-eight hours after each treatment, and in some cases for twenty-four hours just previous to each treatment.

There are occasional reports of some untoward late skin effects concerning which we are as yet unable to speak authoritatively. It is now known that the absence of visible reactive changes, erythema, or pronounced roentgen effect offers no guarantee that skin injuries will not appear later. Skin that has been irradiated is hypersensitive to mechanical, thermic, and chemical irritations. This increased sensitiveness only appears after a latent period. This latent period seems to have been greatly lengthened by improved methods of filtration, but the untoward changes have been encountered as late as a year and a half after irradiation.

Late skin changes may manifest themselves in two ways. (a) There may be a slow development into different grades of a chronic reaction or (b) a long time after the last irradiation the late changes may suddenly appear on the apparently normal skin. Injury to the vessels seems to play an important part in the development of chronic roentgen burns after deep irradiation. Gauss believes the cause of the late injuries is an insufficient filtration of the softer rays. One must also consider the possibility of late injuries of internal organs, especially of the gastrointestinal tract. My experience has been fortunately free from any serious late effects after roentgen treatment of carcinoma of the uterus. In fact, the contrary has been our experience. One patient with recurrent carcinoma of the uterus experienced severe acute enteritis for two or three days following each series of roentgen treatments. In two cases of vesicovaginal fistula the leakage of urine into the vagina stopped for several months. Even though untoward effects of a serious nature should follow roentgentherapy in advanced cases, a local inflammation of the skin lasting from four to six weeks is not too dear a price to pay for a grateful arrest of the disease and a possible, though not probable, cure.

In summarizing the results, it is very difficult to separate the cases which have been treated by roentgen rays or radium alone from those which have been treated by the combined application of these two agents. In the great majority of cases, radium or mesothorium has been used internally and the roentgen rays have been applied to the skin and sometimes by the vaginal route.

The reports by Bumm and Warnekros have been the most enthusiastic. Bumm has also ventured farthest in the administration of gigantic doses of hard rays. An irritation of the skin and the vesicular detachment of the epidermis which healed after three or four weeks, which was practically always experienced by his patients, he did not consider of any consequence. He reports cases of cervical carcinoma as large as the fist without any parametric involvement in which a clinical improvement began within a week and which were symptomatically cured within five weeks. The treatments were given both by the vaginal and the percutaneous methods. The skin overlying the pelvis was divided into twelve to twenty-four squares, through which treatment was given in prodigious doses. After a few more years, it will be interesting to learn the final results in these cases. At any rate, the palliative effects have been extremely satisfactory.

Siellmann reports that of sixteen cases of uterine carcinoma, two were very favorably influenced, and six were materially improved. Forty-one were prophylactically rayed after operation and remained cured.

Von Eiselsberg sums up the effects of roentgen rays in his observations as noteworthy and requiring further endeavor. None of his cases were operable, for von Eiselsberg insists that operable carcinoma must still be removed by operation, and that only inoperable or recurrent cases should be left to roentgen treatment.

Fueth and Ebeler report "favorable" results, especially in recurrent cases, but no mention is made of cases in which they believed cure had been effected.

Scherer and Kelen in 103 cases of inoperable

carcinoma of the uterus treated since 1910 by the roentgen method report twenty-four cases showing a remarkable decrease in the local and general symptoms, in three cases entire disappearance of the tumor, in two cases apparently recovery for more than three years. In addition, two of their apparently inoperable cases became operable after treatment.

And so one might go on through a long list of reports, some encouraging, some discouraging. My intention was to give a brief summary of the results of each of the authors who have published their statistics, but in only a few instances did their statistics cover cases which had been treated by the roentgen rays alone. Usually, as above intimated, the treatment has been a combined treatment, including radium or mesothorium roentgen rays, and in many cases cauterization or diathermia. It seems reasonable that the hot water cautery method as advocated by Percy and others will prove a valuable adjunct in certain of these cases.

In brief, the results of the use of roentgentherapy by the various men who have reported their cases are summed up in some one of the following expressions: "encouraging;" "great advance;" "valuable results;" "a decided advance in the treatment of cancer;" "remarkable results;" "the time is too short to say whether the improvement will be permanent, but . . ." With the exception of a few authors whose very optimistic expressions do not encourage belief in their reliability, all conclusions as to the final results of roentgentherapy and radiumtherapy have been very guarded, although the palliative results have been greater than by any other means. In perusing the great number of publications on the subject, one realizes that the great amount of skepticism especially current in America concerning the results claimed is perhaps justified for the reason that the word "cure" has not been used with sufficient circumspection.

In looking over the literature of competent authors, it is seen that in about 25 per cent of cases of uterine cancer, the temporary effects of the roentgen treatment have been very satisfactory. That the palliative effects have been well worth the while is conceded by all. That these effects are probably as good as can be secured by any other known means is conceded by the majority, but in only a very small percentage of the cases treated has the result been termed a clinical *cure*. From my own experience, I am not able to improve this statement. While our patients have been grateful for temporary arrest of the disease, I have yet to see the first case of definitely demonstrated permanent *cure* of deep-seated pelvic cancer following the application of roentgentherapy or radiumtherapy. Some members of this society can testify to the faithfulness with which the efforts of myself and my assistants have been turned toward the roentgen treatment of uterine carcinoma. That there are recorded cures of cervical epithelioma in the early stages must be conceded, but I have had no successful case of inoperable or recurrent uterine carcinoma treated with the roentgen rays. In no case considered operable has operation been postponed for roentgen or radium treatment.

Considering the great number of cases which have undergone the newer roentgen treatment for uterine carcinoma, the percentage of "clinical cures" is very small. Anatomical examination has shown beyond a doubt the possibility of complete removal of operable and inoperable uterine cancer by irradiation, but what, if any, percentage will be permanently cured cannot be known until after the lapse of eight or ten years. We should not lose sight of the fact that in a considerable number of inoperable and recurrent cases life may be lengthened, and sometimes the patient may be so far restored to health that she is subjectively well and capable of work for years. Pain is relieved, distressing odors are avoided, existence is made tolerable, and the fatal consequences of cancer are postponed so that in many cases the end comes through some quicker, more merciful intermittent affection. We may say with Kienboeck that almost every carcinoma, whatever its kind and location, may be favorably improved by irradiation. But only a comparatively small proportion of cases can be so greatly benefited as to be called clinically cured. To the inquiry as

to the permanency of this clinical cure, time alone can give the answer.

That inoperable cases should be submitted to radiotherapy, preferably the combined application of some cautery method and roentgentherapy and radiumtherapy will not be questioned by anyone. But, shall *operable* cases be subjected to roentgentherapy? Von Eiselsberg says, most emphatically, "No. Operable carcinoma must still be removed by operation. It is a mistake to allow the patient to choose between operation and radiotherapy."

Flatau, on the other hand, advocates the substitution of radiotherapy for operation even in operable cases of carcinoma of the uterus, stating that since December, 1913, he has had a greater number of recoveries than he had with an equal number of cases during the same period of time when he was performing radical operations. At any rate, radiotherapy should be given a chance to show what it can accomplish, for the only final way of deciding between surgery and radiotherapy is, after many years, to compare a large series of cases treated by the two methods.

Meyer takes the position that today carcinoma of the cervix should be surgically treated. He reminds us of the repeated assertion that because the operative statistics are unfavorable we are not justified in concluding that a conservative treatment should be employed. Taking the practical results into consideration, we should do well to continue to operate an operable carcinoma.

In my experience, the results which have thus far followed roentgentherapy of deep-seated malignant affections do not yet warrant us in believing that roentgentherapy affords a means of *cure* in these deep-seated lesions. In the light of our present knowledge, it may be stated as an axiom that the X-ray treatment should not replace or interfere with the surgical treatment of uterine cancer.

Although I have not been able, either from my experience or from a perusal of the literature, to assume an optimistic attitude toward the roentgen treatment of uterine carcinoma so far as a *cure* is to be expected, I would again urge appreciation of the very satisfactory palliative results the radiotherapeutic method affords. These palliative effects have been sufficiently detailed above.

One other question remains; viz., the desirability of post-operative roentgenization. The histological proof of the possibility of permanent cure has been afforded us. The difficulties in the primary use of the roentgen method may possibly be overcome. Be that as it may, we must at present urge that all operable tumors should be surgically removed and that *all cases of malignancy should receive post-operative radiotherapy*. This treatment should be applied as soon after the operation as possible, and as thoroughly as though we believed the disease was still present in its entirety, the patient's sole prospect of cure depending upon our roentgen and radiumtherapy.

NOTE.— There has not been time for the discussion of technical details in this paper. The writer has elsewhere contributed to the literature of this subject a discussion of the technical details. "The Technic of Deep Roentgen Therapy," *American Journal of Roentgenology*, Vol. II, No. 10, November, 1915, p. 811. "Roentgentherapy in Non-Malignant, Deep-Seated Lesions," SURGERY, GYNECOLOGY AND OBSTETRICS, July, 1915, p. 70. "Roentgen Treatment of Deep-Seated Cancer," *The Physician and Surgeon*, October, 1915, p. 442.

RADIUM IN THE TREATMENT OF CARCINOMA OF THE CERVIX UTERI[1]

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IT is unfortunate that so much labor and time are required in attesting the true valuation of a therapeutic agent. Chemists, physicists, physiologists, and clinicians must combine the results of their many labors, and even after their work is completed it is often difficult to make the final deductions properly; to eliminate faulty methods and premature claims of over-enthusiastic pioneer investigators.

The investigation of so-called cancer cures is especially difficult because of the length of time required to check the ultimate results.

Radium has proved no exception to the rule; in fact its novel chemical qualities, its absolutely original physical phenomena and the premature claims as to its wonderful therapeutic properties have doubly confused rather than clarified our knowledge of its actual virtues. It has been used about ten years in the treatment of disease, during which time it has been lauded in the highest terms; abandoned as useless by some, and denounced without trial by many. The first seven years of its use produced only scattering reports. It was in the experimental stage and available for study by only a few clinicians, and it may be said that the statistics of real value have been produced within the past three years, since the methods of application and screening have been better understood, and a larger supply of the element has been available.

From the numerous clinical data now collected, certain well-established facts may be gathered. First among these facts should be mentioned the remarkable influence of radium over uterine bleeding associated with the metropathies, fibromata, and carcinomata. This faculty alone establishes it as an agent of the first rank in the treatment of probably the commonest affection for which the gynecologist is consulted.

There is no longer the slightest doubt that it exerts a powerful influence over cancer-cells. This influence is not the result of cauterization, as many pathologists would have us believe, nor is it because of any selective action on cancer-cells, but rather its effect on all cell life. Its effect is well described by Burnam, who states that "it can be assumed that radiation deleteriously affects all living tissue, but under this injurious influence the normal tissues are preserved because the fluids and the protective agencies of the body are all constructed to help the normal tissues, and that the pathologic tissues disappear because, weakened by radiation, they are unable to withstand the normal protective mechanisms of the body. This readily explains why a similar growth in different individuals will react differently or not at all to radiation; why slight radiation will effect marvelous changes in one case and show just the opposite changes in another. It must also be borne in mind that certain normal tissues are more resistant than others and that the latent period of radiation may be influenced by all of the above-named factors and promptly points to numerous problems yet to be solved by radiophysicists. Whether the solution of these problems depends upon earlier treatment, larger dosage, more efficient screening, or by combining radiation with operation or other therapeutic agents, remains for the future to solve."

There is another point which must be kept constantly in mind by the clinician; viz., his duty and obligations to the already proved principles of the surgical treatment of cancer.

Surgery is the only treatment so far known that offers a permanent cure for cancer in the early stage of the disease. No discussion which might detract from the high esteem in which surgery is held should be allowed to filter out to the inexperienced practitioner and particularly to the public at large. Until something more satisfactory than surgery is

[1] Presented in the symposium on "Cancer of the Uterus," at the meeting of the Chicago Gynecological Society, December 17, 1915.
(For discussion see p. 502.)

positively proved, we must unite in the common cause of educating the public to the importance of early surgical treatment, remaining in the meantime in a receptive attitude toward the efforts of investigators to reach the common goal by other avenues. We must agree that we have about reached the limitations of operative technique in cancer eradication. No one may venture farther than the present established technique of breast amputation or radical hysterotomy. If we increase our percentage of ultimate cures it will be by earlier operation or by combining other therapeutic agents with surgery.

The most promising agent so far known is radiation, either by special X-ray apparatus or radium. Both agents are scarcely beyond their infancy and their wonderful properties seem to be manifold and lead into divers ramifications.

It is not difficult to define my attitude toward radiumtherapy after the above remarks. So far I have employed it solely as an adjunct to surgery. I have not been satisfied with the results of radical operation, not to mention the 60 to 70 per cent who come so late for treatment that even palliative measures are often useless and burdensome to the doomed patient.

As my experience with radical operation increased, the percentage of cases in which I advised it gradually decreased. I no longer recommend it in the so-called borderline cases, believing that such formidable treatment, with its primary fatalities and subsequent morbidity, does not give sufficient returns for the risk incurred. It was with the idea of increasing the permanent results obtained by surgery by the combination with radium, the conversion of inoperable into operable cases, and last but not least the amelioration of the suffering of the hopeless cases, that I determined to try radium.

I regret that I can offer as yet no statistics that might show that my operative results have been improved by the use of radium prior and subsequent to operation. Such conclusions must necessarily be based upon a large series of definitely classified cases by the same operator doing the same type of operation and following the cases for a longer period than any one has yet been able to extend their observations. Prophylactic raying after operations is now fairly well established on a rational basis. The only statistics at my convenience bearing on this point are those of Gauss, who reported that of 21 operated upon and rayed, 20 had remained free from recurrence up to six years after operation, while their previous experience showed that in 60 per cent of cases operated upon without radiologic treatment the disease showed evidence of recurrence within one year.

I also regret that I cannot produce practical personal evidence that preliminary application of radium will convert inoperable into operable cases. Improvement has been so gratifying in four of my cases that I have repeatedly urged hysterectomy, but notwithstanding my strongest arguments, three positively declined, stating that they had improved so satisfactorily that they were willing to assume the risk. The fourth has agreed to submit to operation within a few weeks. I may add that many good authorities differ as to whether or not advanced cases become operable under radium therapy. Whether or not the accompanying parametrial involvement which disappears under radiation is of malignant or inflammatory origin cannot be determined without operation and offers another serious difficulty in diagnosis. There is no doubt that radium applications prior to operation add some difficulties to the operative technique. The widespread connective-tissue changes would necessarily make the usual dissection exceedingly tedious and must be taken into consideration when it is decided to operate after radium treatment.

It is the tendency at present to operate on more of these cases than formerly, so it will be only a matter of time before the value of the combined treatment is fully known.

The results I shall present are derived from the application of radium in 26 cases of inoperable cancer of the cervix uteri and recurrent cancer following hysterectomy that have come under observation since May, 1914. All have been followed up to December

1, 1915. The list is small and the length of time that has elapsed too short to permit of practical deductions except as to the primary results of radiumtherapy. It permits me, however, to state most emphatically that radium is a great boon to patients suffering from inoperable and recurrent cancer of the cervix uteri. I have seen large inoperable carcinomata fixed in the pelvis entirely disappear within a month and the patient's general condition correspondingly improve. Bleeding was almost invariably controlled within two weeks and the foul discharge disappeared almost as rapidly. Even in cases in which the local process did not respond the bleeding was checked, the discharge changed in character, the pain usually decreased and the general condition improved for a short period. Fifteen inoperable cases were treated solely with radium. They were far advanced, showed the usual cachexia, and several were not good risks even for simple cauterization under anesthesia. Four have died and two are slowing succumbing to the disease. Five are apparently free subjectively and objectively of disease. Among the five who are apparently well are two of the earliest cases and the others were treated about nine months ago. The primary results were almost uniformly good when the condition at the time of treatment is considered.

Four cases did not respond to treatment. They were far advanced, the vagina, bladder, and rectum being involved. Bleeding was checked and the pain reduced but they gradually lost ground and died within two months.

The first case in this series was treated in May, 1914. She writes November 29, 1915, that she had a slight hæmorrhage in March, 1915, but it lasted only a day. She has been comfortable since but has lost some weight. Four in the series showed evidence of returning trouble about 6 months after treatment, but responded to further applications. It is too soon to tell how long they will remain free from symptoms.

It is interesting to observe the remarkable deodorizing action of radium. Sepsis is the commonest complication of advanced cervical cancer and the attending foul discharge is the most disagreeable feature both to the patient and her attendants. Ten days after radium applications the odor begins to disappear and the temperature, if present, usually subsides. This effect alone has prompted several patients to state that the treatment was worth while, whatever the final results might be.

The relief of pain is usually as marked as the control of discharges. Pain is usually due to the septic complication and consequently subsides as the local process improves. The subsidence of pain, however, does not depend entirely upon this factor, as I have seen patients abandon opiates within 24 hours after the first application.

CASES CAUTERIZED PREVIOUS TO RADIUM TREATMENT

Six cases has been excochleated and burned one to five months prior to radium treatment. In every instance the disease was rapidly reappearing when radium was first applied. The first case was treated in May, 1914. She was cachectic, suffered intensely, and had an exceedingly offensive discharge. The bladder was involved, the rectal wall was infiltrated and the remaining parametrial structures fixed. She improved rapidly, gained 17 pounds in weight, and the local process completely disappeared. She remained well until October, 1915, then died after a brief illness. Her physician stated that no evidence of trouble could be found in the vaginal vault. Since she had excruciating pain in her left hip for two weeks before her death, it is to be believed that she died of metastases remote from the vaginal vault. Three of these cases are apparently free from disease twelve months after treatment.

Just at this point it is apropos to discuss whether or not it is better to burn or use the curette on sloughing masses before applying radium.

My experience leads me to believe that it is not the best mode of procedure. I am positive that it required a longer time to check the local symptoms and the subsequent histories do not show that they remained well any longer for having had the preliminary cauterization. Preliminary cauterization re-

quires anæsthesia and is attended by no little discomfort and certainly retards the primary effects of radiation. My experience is corroborated by others, especially Burnam, who recently stated that he no longer cauterized and curetted sloughing masses as a preliminary measure.

RECURRENT CARCINOMA AFTER HYSTERECTOMY

I have applied radium to malignant areas reappearing in the vaginal vault after hysterectomy in 6 cases. These cases are utterly hopeless from a surgical standpoint and unfortunately are much less amenable to radium-therapy than primary processes. In four cases the growth promptly responded to treatment but the results cannot yet be known owing to the short period elapsed since the applications were made. The first case presented a fungus bleeding mass in the vault two years after I had performed hysterectomy. Radium was used in December, 1914. She was entirely free of local symptoms when examined December 1, 1915, and her general health is excellent. Two other cases are apparently well six months after treatment. In one case the mass disappeared, but the patient died soon after from an infected kidney.

In another instance local masses have responded twice within the past year to applications, but her general condition is gradually waning.

I have related in a general way these personal experiences to show just what my results with radium have been so far. As you will see they do not prove that radium will cure cancer, for the most favorable cases have not been followed yet two years. They prove conclusively to my mind, however, that cancer of the cervix is profoundly influenced by radiation in cases that are hopeless surgically and that the results were accomplished with a minimum of discomfort to the patients. I may further add that the results so far are superior to any other method I have used in similar cases.

The primary result is often beyond the hopes of its most enthusiastic supporters. Bedridden sufferers have been given a new lease on life and some have been improved to the extent that surgery might be beneficial when it was originally useless. The remarkable primary results caused many early workers to report cures which were unfortunately only temporary symptomatic cures. The same test of time must be applied as in surgical statistics before they are transferred to the cured column.

One point in favor of radium which should not be overlooked in the final analysis is that the present statistics will be based upon material that has passed beyond surgical relief before radium is used. If radiation can show even a fair percentage of cures at the end of five years, its usefulness will be fully established in a class of cases not amenable to any other form of treatment. The chief point of interest after all is the duration of radium treatment. The only recent available statistics that might throw light on this phase of the subject are those of Kelly and Burnam. Schmitz has also published some extremely interesting figures, but like my own, the cases can be followed only since April, 1914.

The statistics of Kelly and Burnam probably contain more cases observed over a longer period than any other single clinic can show at present. They report 57 clinical cures; 35 cases of original inoperable cancer of the cervix uteri and vagina, and 18 cases of originally inoperable recurrent cancer. One cure has lasted 6 years; 3 for over 4 years; 4 for over 3 years; 5 for over 2 years; 29 for over 1 year, and 15 for 6 months. If this list is again summarized two years hence, we may begin to learn something of the ultimate results.

Cheron and Duval's statistics approach approximately those of Kelly and Burnam in number and length of time observed and practically coincide with the latter's figures.

TECHNIQUE

There still exists a wide difference of opinion as to the proper usage of radium in treating uterine cancer. Some believe that the problem is solved when sufficient radium can be made available to give massive doses hitherto impossible owing to the scarcity of the agent.

Schauta, Kelly and Burnam, Kroenig, Wickham, and others believe in massive dosage while other equally well-known observers believe that smaller amounts applied for a longer period will accomplish the same results.

What the final conclusions will be remains to be seen, but it is generally agreed that less than 50 milligrams of the *radium element* should not be employed, lest the growth be stimulated instead of causing the necessary necrosis.

Puich, who has large quantities of radium at his disposal, finally decided upon a dosage of 50 to 100 milligrams. Schmitz used uniformly 50 milligrams giving 6 to 8 séances of from 10 to 12 hours. The course is followed by an intermission of three weeks. If examination then reveals an apparent cure, two or three applications of 500 or 600 milligram hours of radium element is given every second or third day, followed by another interval of three weeks.

This has been practically my plan with the exception that I use from 75 to 85 milligrams of the radium element and endeavor to give from 3,000 to 5,000 milligram hours within a week or ten days. One month later further applications are made according to the indications.

No one can doubt that cancer of the cervix can be entirely eradicated by radium. Unfortunately it is not the cervix *per se* that controls the ultimate termination; the outlying cancer areas in the broad ligaments and the glandular metastases really control the situation. If the penetrative powers of radium can be made to reach the outposts of the disease, its value will be inestimable.

Bumm's widely quoted experiments which showed that the limit of the γ-ray efficiency (in tissue) was about 4 cm. is now very correctly questioned by Burnam, who states that it is possible to radiate any distance by proper distribution of the applicators, all of which goes to show that the seemingly insurmountable obstacles are being overcome as experience increases. To prove that cancer can be anatomically cured will be much more difficult than any phase of the work so far accomplished. It will require not only long years of observation, but it will require as well a microscopical study of serial sections of outlying tissues removed at subsequent operations and at post-mortem findings. This is a task stupendous in itself and can only be solved in the manner recently illustrated by Schmitz, Cheron and Rubens, Duval, and others.

The scope of this paper does not permit of much more than a statement of my personal experience. I cannot offer any general conclusions other than to say that radium has a wide field of usefulness, the real value of which can be estimated only after painstaking collective studies. It has no field absolutely to itself but is merely a therapeutic agent which should be used in common with other well-established methods of treatment.

PROPHYLAXIS OF UTERINE CANCER[1]

By THOMAS J. WATKINS, M.D., F.A.C.S., Chicago

THERE are no means to determine that cancer has or has not in a single instance been prevented. This paper must consequently deal with probable or possible means of prevention of cancer of the uterus.

The possible relation of traumatisms of the cervix to cancer. There has been and continues to be a belief by many that traumatisms of the cervix are at times an etiologic factor in the development of cancer. Emmet was of the opinion that laceration of the cervix was a contributing cause of cancer, as he said: "I have never known cancer to occur in women who have not been pregnant." A. Martin states that laceration and syphilis of the cervix are predisposing causes of cancer. Cullen's conclusion from the study of cases of cancer is that injuries incident to labor have a potent influence in the development of squamous-cell cancer of the cervix.

The facts that cancer occurs in women who have not borne children and occasionally in virgins, that it frequently begins in the glands of the cervix far distant from the vaginal portion and at times does not extend to the vaginal surface until late in the disease, are proofs at least that there is no constant relation between traumatisms of the cervix and cancer. There are no statistics that are of much use in the study of this phase of the subject; for example, as to the frequency of cancer occurring in extensive erosions of the cervix, or resulting in cases following trachelorrhaphy or amputation of the cervix.

When a cancer is found with an erosion, it is usually impossible to determine if the erosion antedated or followed the cancer. Cancer is not uncommonly found in the absence of erosions. Cases are occasionally seen with an extensive eroded surface on the cervix where cancer cannot be excluded or determined, except by microscopic investigation.

From the meager knowledge which we have of cancer, one must infer that the irritation and circulatory disturbances, resulting from traumatisms, can be the only possible causative factors in the development of cancer of the cervix and that traumatisms of the cervix are not a frequent contributing cause of cancer.

Should erosions and extensive glandular degenerations of the cervix be treated as a possible prophylaxis of cancer? The gynecologist is frequently consulted relative to these problems. It would be highly desirable to have some standard established for guidance, as undoubtedly many unnecessary operations are done for this purpose. On the contrary, I am convinced that many erosions of the cervix are neglected. An erosion of the cervix should receive attention for the same reasons that abraded surfaces should be treated when afflicting other parts of the body. It has become a habit to neglect them. They are probably most important as focal infections, but may be etiologic factors in cancer, as is an erosion of the lip, tongue, nipple, etc.

Many cases of erosion are amenable to medical treatment. The more extensive ones, with deep lacerations and glandular degenerations, require operative treatment. The operation in the bad cases, in women that will probably not have pregnancies, should be a high amputation, including most of the glands in the cervix. It would seem that the presence of scar-tissue in the cervix is in itself of not sufficient importance in the etiology of cancer to need serious consideration. From a theoretical viewpoint, the problem would always seem to be easily determined, but in practice one occasionally sees cases where the question of a plastic operation or a hysterectomy is a serious consideration.

Hæmorrhage after the menopause. Hæmorrhage occurring after the menopause has been established for some time should as a rule indicate hysterectomy. Hæmorrhage at that time should be considered cancer. If cancer is not found the operation is justified

[1] Presented in the symposium on "Cancer of the Uterus," at the meeting of the Chicago Gynecological Society, December 17, 1915.
(For discussion see p. 502.)

as a prophylactic measure. Cancer is the *common disease* that produces bleeding from a uterus that has become senile and atrophic. We believe that fewer mistakes in diagnosis are made by considering all of this group cancer than by the use of other known means for diagnosis in individual cases. This has been our practice for some years and the results have been highly satisfactory.

We share the opinion expressed by many and especially emphasized by Bloodgood that incisions into and curetting of cancers should be avoided. In only a small percentage of our cases has it been considered advisable to incise or curette for diagnosis of cancer. When these means are used a frozen section should be made and immediate operation done if a carcinoma is present. Bloodgood's study of cases would indicate the great importance of *immediate operation* after incision into cancerous tissue.

Tumors of the uterus. Morris H. Richardson[1] contributed a valuable paper in which he strongly advocated the removal as a rule of all tumors as a prophylaxis of cancer. This principle of treatment, we believe, should apply to uterine tumors.

The dangers of malignant degeneration in fibroid tumors of the uterus have been found by statistics to be between 3 and 5 per cent. The dangers incident to operative treatment have been reduced so that they can conservatively be placed at 1 per cent. The dangers from malignant disease in fibroids are therefore three times more than from operation.

All uterine tumors should be removed as a prophylaxis of cancer, irrespective of other indications.

[1] J. Am. M. Ass., 1909, p. 1553.

POST-OPERATIVE TETANUS[1]

By KELLOGG SPEED, M.D., F.A.C.S., Chicago

THE habitat of the tetanus bacillus and its spores is widespread. The bacilli have been found in the bottom of mountain lakes in Switzerland, in the draggings of the Dead Sea, on the arrowheads of aboriginal natives, in the bilge-water of ships, and in the clothes and on the skin of human beings. Commonly we expect to find them in street dust, fertilized soils, and in the fæces of animals.

In 1887 Croussard[2] reported an attack of sickness resembling tetanus in three individuals who had eaten beef infected with tetanus. Two of these patients died. In 1890 Sormani[3] found tetanus bacilli in the fresh stools of several different animals. Sanchez, Toledo and Veillon[4] studied the dejecta of healthy horses and cattle to determine the presence of tetanus organisms in them and this year Noble[5] has repeated the earlier experiments on a more extensive scale. He examined the fæces of 61 horses, 21 cows, and 1 guinea pig for tetanus spores and organisms. Of 61 horses 11, or 18 per cent, showed tetanus organisms. None of the cows gave positive result for tetanus, probably because they were examined in the winter while being fed on ensilage. The one guinea pig examined showed tetanus in the stools. Sanfelice[6] found tetanus spores in 7 out of 23 normal guinea pigs. Pizzini found that about 5 per cent of human beings showed tetanus bacilli in their stools, the average varying from 2 per cent to 20 per cent, the higher proportion existing in men who worked about horses and stables.

Carnivora as a rule have a relative immunity for tetanus which is caused according to Walsh[7] by a combination of bactericidal and phagocytic action on the part of the host. This immunity may be expressed moreover by the following:

[2] Etudes à l'appui de l'origine infect. du tétanus. Thèse de doct., Paris, 1887.

[3] Zentralbl. f. Bakteriol., 1890, vii, 250.

[4] Zentralbl. f. Bakteriol., 1891, ix, 18; Semaine méd., 1890.

[5] J. Infect. Dis., 1915, xvi, 132.

[6] Ztschr. f. Hyg. u. Infectionskrankh., 1893, xiv, 234.

[7] Am. Vet. Rev., 1914, xlv, 333.

[1] Read before the Chicago Surgical Society, January 7, 1916. (See discussion, p. 496.)

1 gm. of horse is destroyed by X toxin.
1 gm. of goat is destroyed by 2X toxin.
1 gm. of mouse is destroyed by 13X toxin.
1 gm. of rabbit is destroyed by 2000X toxin.
1 gm. of hen is destroyed by 200,000X toxin.

Experimental work on the fate of tetanus bacilli and toxin in the alimentary tract of animals must be inquired into in so far as it concerns the subject we are discussing. In 1899 Carrière[1] investigated the disposition of tetanus toxin introduced into the alimentary tract of animals, and he proved that enormous doses of tetanus toxin could be introduced into the stomach of animals without causing death, but these animals did not become immunized and their blood serum had not antitoxic properties. It was also determined that ptyalin destroyed the toxin, that gastric juice attenuated it, and that bile and pancreatic juice destroyed it totally. The intestinal epithelium did not seem to influence it. Rabinowitsch[2] concluded after some experiments that the higher the acidity of the gastric juice, the greater the numerical destruction of tetanus bacilli immerged in it, and concluded also that it was dangerous for persons to carry tetanus bacilli in the alimentary canal. Vincent[3] in 1908 studied the action of the large intestine on tetanic toxin. He introduced 3,000 units of toxin into the large bowel of a guinea pig with no untoward result. Thereafter he performed laparotomy on a guinea pig, tied off 10 to 15 cm. of the large bowel and injected a like quantity of toxin into this isolated portion. The pig's abdomen was closed, the animal was kept in warm surroundings for two to three hours and the piece of bowel was removed. After being macerated, the filtered liquid was found to be non-toxic; there was not a trace of tetanus toxin. Carrière, mentioned previously, believed that the ordinary intestinal flora attenuate but do not destroy tetanus toxin. To determine this action, Vincent made bouillon cultures from intestinal contents and, after 24 hours' growth, mixed into them a certain quantity of tetanus toxin. This mixture was allowed to stand two hours and was then filtered. The filtrate produced tetanus in a guinea pig. The conclusions he arrived at were that the secretion of the small intestine is very antitoxic, that of the large intestine is less antitoxic for tetanus toxin, and that the toxin introduced into the rectum is destroyed. Breton and Petit[4] also endeavored to determine the permeability of the large intestine of guinea pigs to tetanus toxin by injecting up to 3,000 times a lethal dose into the large intestine via the rectum. There were no deaths after these injections. They concluded that the toxin was either destroyed or was incapable of traversing the intestinal mucosa. They took 500 times a lethal dose of tetanus toxin, incubated it with rectal contents of a guinea pig and after forty-eight hours injected the filtered liquid into the muscular tissues of a guinea pig with fatal results after 16 days. From their experiments the conclusion seemed warranted that the intestinal flora exerted a partially destructive action on tetanus toxin but the mucosa had no influence. The permeability of the mucosa to the toxin was thoroughly tested by using six guinea pigs, injecting each at five day intervals with four successive doses of 3,000 times the lethal dose of toxin. Nine days after the last injection they were able to demonstrate tetanus antitoxin in small quantities in the blood taken from the animals. By using rectal injections of antitoxin they believed that animals could be immunized against tetanus.

In the present year Sinigaglia[5] has reviewed the subject of tetanic infections via the blood stream as found in other bacteræmic diseases. In tetanic infections the bacilli have been found in the milk, lymphatic glands, muscles, and nerves. Nicolaier[6] found the bacilli in the sciatic nerve and spinal canal, Haegler[7] in the medulla oblongata of a fatal case, and others as Reinhardt and Assim[8] have found them in the blood after death, obtained cultures and positive inoculation results in animals. Schnitzler[9] obtained the bacilli from a lymphatic gland and secured positive

[1] Compt.-rend. Soc. de biol., Par., 1899.
[2] Arch. f. Hyg., 1907, lxi, 103.
[3] Compt.-rend. Soc. de biol., Par., 1908, 162.
[4] Compt.-rend. Soc. de biol., 1908, 160.
[5] Riforma med., 1915, No. 17, 454.
[6] Virchow's Archiv. f. path. Anat., 1892, cxxviii.
[7] Beitr. z. klin. Chir., 1889, v, No. 1.
[8] Zentralbl. f. Bakteriol., lxix, 583.
[9] Zentralbl. f. Bakteriol., xiii, 679.

results by animal inoculation, and Hohlbeck[1] obtained positive cultures from the blood of a patient five hours before death from tetanus. The only case in which tetanus bacilli were demonstrated in the blood of a patient who recovered from the attack was reported by Vanni and Giarré.[2] Sinigaglia's case terminated fatally but positive cultures were obtained both from the site of injury and from blood taken from the arm. He believes that the bacilli and spores can get into the blood stream to cause a toxæmia and possibly the rheumatic form of the disease without multiplying or localizing.

Can animals become permanent tetanus carriers? Noble's work seems to show that they can. In his experiments at the time of feeding tetanus bacilli and spores a capsule of carmin was given. The carmin was eliminated within 24 hours, but tetanus spores were not found until the sixth day in the dejecta from the horse, although they may have been present before that in too small numbers to give positive cultural results. One horse continued to give off spores for many months while another ceased after the fourteenth day. The stools of control horses were negative. This one horse may have been a tetanus carrier. Quantitative tests showed that tetanus spores may be found in the fæces of animals carrying them in amounts from 0.1 to 0.01 gm., but not in smaller amounts. Failures may be caused by cultural methods. We can believe then that tetanus bacilli may be present in the fæces of normal animals and may not be detected except when present in large numbers. The bacilli may multiply in the intestines of some animals which favor their growth and these animals may become tetanus carriers.

As a final biologic consideration we must understand the requirements for the development of tetanic infections which produce symptoms and death. The pathogeny of tetanic infections is a complex phenomenon which according to Vaillard[3] must have the simultaneous help of several factors. This is verified inasmuch as pure tetanus spores freed from tetanus toxin of the culture and injected by the millions into the healthy tissue of an animal are harmless. When the spores are deprived of the pre-existing toxin they are devoured by phagocytes, but if some of the same spores in small quantities are injected into the same animal's tissues when the spores are artificially protected against phagocytic action, tetanus is produced. As an example of this requirement a guinea pig, an animal very susceptible to tetanus, will resist large numbers of toxin-free tetanus spores introduced subcutaneously or intraperitoneally. These animals, however, will succumb to tetanus when but a few spores are injected mixed with unsterile sand or enclosed in a collodion sac. The foreign material with the spores acts as a barrier to the leucocytic action of the host, tetanus toxin is developed, and the animal dies from the absorption of the diffused poison.

Let us consider these biologic facts in relation to tetanus in man. For the development of tetanus in man one must have an infection with the specific germ and favorable conditions for its growth in accordance with the requirements described. Simple injuries, superficial and practically aseptic in character, do not favor the growth of tetanus spores. Trauma alone is not a sufficient aid. When tetanus develops in man we must look first for other auxiliary factors in the infected tissue, such as burning, extensive crushing or hæmatoma formations, all of which may be called traumatic results. Secondly, we must look for associated micro-organisms. Necrotized tissue from burns, crushes and ligated areas and collections of blood within tissues, favor the growth of tetanus because the usual leucocytic resistance is held at bay.

Tetanus organisms are usually encountered in soils or manure mixed with many other micro-organisms, all of which may be expected to enter a soiled wound under equal chances for growth. Some of these added bacteria favor tetanic growth, others do not, a fact easily verified clinically when the enormous number of infections are considered in comparison with the few tetanic developments. In man we must have an inflamed wound with more or less evidence of suppuration

[1] Deutsch. med. Wchnschr., 1903, x, 172.
[2] Riforma med., 1887, Aug.
[3] J. State M., Lond., 1914, xxii, 513.

for the growth of tetanus. Animal experiments have verified these statements. An amount of garden soil infected with tetanus is divided into two portions and moistened. One part is injected into a guinea pig; it dies of tetanus. The other part is heated to 80°C., a point which does not destroy tetanus spores, but does other non-sporulating organisms. After injection of the heated soil no local lesion of importance results and no tetanus develops. If later favorable micro-organisms are added to heated soil and injections are made of it into susceptible animals, tetanic death results. In practical treatment of wounds antiseptic irrigations and applications may not kill the tetanus organisms but they do kill or greatly reduce in number associated organisms which assist in tetanic growth, probably by consuming oxygen.

Tetanus in civil practice has become almost eradicated by the prophylactic use of antitoxin and the antiseptic treatment of dirty, contused and lacerated wounds. Cases of non-traumatic tetanus still persist, especially the unforeseen post-operative cases. Let us apply the pathogeny of traumatic tetanus to these other forms of non-traumatic tetanus.

Natonek[1] believes that spontaneous or non-traumatic tetanus must be instituted from either pathologic or physiologic processes, and that the usual entrance of the infection is through the outer covering of the body, seldom through the internal organs. Wounds of the navel in the newborn and post-partum and abortion infections in adults may be considered as physiologic wounds. Pathologic wounds are found after injections, vaccination, and after operations.

The following forms of non-traumatic tetanus are possible:

1. Cryptogenetic or rheumatic tetanus, which occurs as a delayed infection after a trauma or an unknown atrium of infection.

2. Tetanus after skin lesions. These may be very simple and unsuspected as an infection atrium. Kirmisson[2] has reported two cases, and Broca[3] one case of fatal tetanus in a child from the use of felt pads to compress the spine in the treatment of scoliosis by Abbot's method; small skin excoriations made by pulling the felt pads under the body encasements of plaster became the seat of tetanic development. Organisms were found on the felt. Sterilization of the felt before use is now considered necessary. The skin lesions may be—

a. In connection with mechanical lesions, such as ulcers of the leg, infected tumors, nasal excoriations or paraphimosis;

b. In connection with bacterial skin lesions;

c. in connection with thermic lesions as burns or frost-bites.

3. Tetanus from the respiratory and digestive tracts.

This includes also infections through the ear, a few of which are known. Through a healthy lung the infection is not possible, but in chronic bronchitis, bronchiectasis or lung-abscess cases have been found. Infection via the tonsils is known. Luckett[4] has recorded a fatal case of tetanus in a child with the point of infection in the cavity of a tooth. Tetanus bacilli were found among other organisms in the tooth and their character was proved by inoculation experiments. Intestinal infections in tetanus carriers may have been the cause of many of the cryptogenetic or rheumatic cases, as I believe they have been in many of the post-operative cases. Most writers have considered them a remote possibility. A few cases in connection with typhoid fever, pericæcal abscesses or fæcal impactions in the rectum have been recorded.

4. Tetanus after injections, from hypodermic needles, from infection carried in from the skin surface or from mixtures injected, such as gelatine.

5. Tetanus after vaccination. Usually from secondary infection by tetanus bacilli, rarely and practically never at this time from the vaccine. McFarland[5] collected 14 post-vaccinal tetanic infections, all secondary. Wadsworth reviewing the cases of tetanus in Philadelphia for the 25 years from 1885 to 1909 found 12 post-vaccinal cases, 9 of which

[1] Zentralbl. f. Grenzgeb. d. Med. u. Chir., 1913, xvii, 196.
[2] Bull. Acad. de méd., Par., 1914, lxxi, 746.
[3] Arch. de méd. d'enf., Par., 1914, xvii, 601.
[4] Med. Record, 1910, lxxvii, 319.
[5] Lancet, Lond., 1902, September 12, and Proc. of Phila. County Med. Soc., 1902.

were doubtful as to the origin of the infection and were probably secondary, while 3 seemed to be primary infections from the vaccination.

6. Tetanus after operation.

In this class I wish to place tetanic infections occurring after elective operations in cases which are classed as clean from the first. The possible avenues of infection are: (1) the operator's hands, (2) the instruments, dressings, and ligatures, (3) air infection, and (4) the patient himself. This last source has been considered remote, and Matas[1] was the first to call serious attention to it. A large majority of the reported post-operative cases in the pre-aseptic and early aseptic era were connected with operations in the female pelvis. Olshausen[2] in 1886 collected 49 tetanic cases occurring after ovariotomy. Picherrin[3] in 1901 collected 98 cases and Zacharias[4] in 1908, 72 tetanic cases after operations on female genitalia. Other large collections especially those made by veterinarians followed castrations. A few cases followed operations other than those of gynecologic character. Brunner[5] reported a case after a goiter operation, injection of the wound secretion in a mouse causing tetanic death. Wilms in the ten years from 1868 to 1879 found 5 cases after herniotomy. Calinescu, quoted by Natonek, reported 4 cases after breast amputations, and Santos-Fernandez[6] a case after enucleation of the eye. Natonek states that there was less post-operative tetanus in the two decades preceding 1900 than in the decade to 1909. Undoubtedly there were more operations in this last decade and probably the increase in the number of cases can be attributed to the larger number reported and not kept secret by many operators.

Because post-operative tetanus has not disappeared from aseptic surgery operators have been forced to seek a cause for the infection on which to lay the blame. Naturally animal ligatures—catgut—have become the cynosure. Two points in that connection are worthy of attention. In the early days of catgut use for buried suture and ligature, very little was ever said or noted concerning tetanic infection from it. In the first decade of this century, in spite of the enormous amount of catgut used there are only some sixty cases of tetanic infection which are even remotely attributed to its use. In 1898 Koch[7] reported a case of post-operative tetanus in a woman on whom a supravaginal amputation of the uterus had been performed. He found an abscess with a piece of catgut in the contents. Kuhn[8] in 1906 detailed elaborate directions for the only safe method of rendering catgut sterile for ligature purposes. Two of the 72 cases previously referred to reported by Zacharias occurred during recent aseptic surgery following removal of ovarian tumors which were adherent to the other abdominal contents and because they occurred within ten days of each other they were considered as being caused by inborn infections. Jerie[9] studied an epidemic in the Prague clinic in 1897 and 1898 and 4 cases which occurred in 1906 after gynecologic operations. The catgut was not considered at fault. Leyden and Blumenthal in *Nothnagel's Handbuch* reported two fatal cases after hysterectomy, and Meinert[10] reported 3 post-operative cases, one of which was supposed to be caused by a Bozemann's uterine catheter. Bertarelli and Bocchia[11] showed that sterile catgut could be prepared simply. In the same year (1909) Worthe showed the lack of tetanus danger in raw catgut by animal experiments. Raw catgut was placed subcutaneously in 680 mice, 7 of which died within four weeks, none of anthrax or tetanus. Bocchia[12] examined 200 strands of raw catgut bacteriologically with negative results. Tourneau[13] in 1904 had recorded a case following a herniotomy, onset occurring on the ninth day after operation, but the patient had sustained a gunshot of the foot on the day before herniotomy. The gunshot wound

[1] Tr. Am. Surg. Ass., 1909.
[2] Billroth's Handb. f. Frauenkrankheit. 1886.
[3] J. méd. de Bordeaux, 1901, 52.
[4] Muenchen. med. Wchnschr., 1908, 5 and 7.
[5] Beitr. z. klin. Chir., 1891, xii.
[6] Rev. gén. d'ophth., 1896.
[7] Deutsch Ztschr. f. Chir., 1898, xlviii.
[8] Muenchen. med. Wchnschr., 1906, xli, 41.
[9] Mitt. a. d. Grenzgeb. f. innere Med. u. Chir., 1908, xix.
[10] Arch. f. Gynaek., 1893, xliv.
[11] Zentralbl. f. Bakteriol, 1909, .l.
[12] Riv. d. ig. e san. pubb. Roma, 1910.
[13] Deutsch. med. Wchnschr., 1904, 10.

had been opened and pieces of shoe removed from its depths. Reinhardt and Assim[1] reported a fatal case of tetanus after herniotomy on a 19 year old male. A small abscess was found from which smears and cultures were made showing tetanus bacilli. Virulent tetanus bacilli have been found in small granulating wounds as late as two and one-half months after tetanus symptoms had disappeared.

Richardson[2] reported 2 cases of post-operative tetanus, one after an omental hernia and one after a gall-bladder operation, and collected in all 21 cases in which the infection had been laid on the catgut used. It was believed that many of these cases occurred in regions in England in which there were tetanic sheep, or sheep infected with louping-ill described by Hamilton. This sickness is characterized by trembling muscle spasms and occurred mostly in the spring of the year. Consequently the post-operative cases in man were attributed to infection from the sheep gut, but on investigation it was found that the sheep gut used as ligatures had all come from Germany and from 14 of the 21 cases the gut had been examined. Four contained a bacillus resembling tetanus but animal experiments with the organism proved negative.

In surgery, operations other than laparotomy occur twice as often as opening the abdomen, and more ligatures are used in them, but in 19 of the 21 cases collected by Richardson the operation was a laparotomy and handling or suturing of the bowel was performed. Richardson cited the experience of one operator who on a certain morning performed 5 laparotomies, using the same preparation of catgut. Patients number 3 and 4 in this series, a gall-stone case and an appendectomy respectively, developed tetanus, but the other cases did not.

In 1909 Matas[3] called attention to the risk of tetanus infection in operations on sterile tissues in which post-operative asepsis cannot be assured. Operations on those parts of the body exposed to fæcal contamination are the doubtful ones because of infection derived from fæcal discharge. The genito-urinary organs of both sexes, the anorectal regions, the sacrococcygeal region, and the inner surfaces of the thigh or legs or any other part of the body which might be contaminated, lie in this class. After two personal cases Matas advised abstinence by the patient for several days prior to operation from such foods as might carry tetanus. Raw vegetables and other food as lettuce, celery, cabbage, watercress, radishes, tomatoes, etc., and raw fruits as strawberries, blackberries, etc., must be removed from the diet and a free catharsis instituted for three or four days previous to operations on the areas named previously. If this preparation cannot be made, Matas advised a prophylactic dose of antitetanic serum. By these means it was hoped that the occasional case, 1 in 10,000 or 15,000 might be saved from a post-operative tetanus. Lucid[4] reported a case of post-operative tetanus after oophorectomy and endorsed Matas' instructions for preliminary cleansing of the alimentary tract. It is believed that the lowering of the peritoneal resistance by operative handling and separation of adhesions permits the emanation of tetanus bacilli which lie within the canal, out into the damaged tissues which in normal state would be able to resist.

Atkinson in 1915 reported a case of post-operative tetanus following removal of hæmorrhoids and found that there were but six other cases, those of Matas,[5] Shaw,[6] Wood,[7] Souchon, Gerrish and de Nancrede (discussion of Matas' paper). He omitted Jacobson's case in the same discussion and that of Wadsworth, who found one case after hæmorrhoids in his examination of Philadelphia[8] records.

Through the kindness of Dr. Irons I have been informed of three of the following six cases. Two cases occurred in surgical service at the Cook County Hospital, Chicago.

CASE 1. Abdominal hysterectomy for fibroids, salpingo-oophorectomy, appendectomy. Onset of

[1] Zentralbl. f. Bakteriol., 1909, 49.
[2] Brit. M. J., 1909, i, 948.
[3] Tr. Am. Surg. Ass., xxvii, 40.
[4] Buffalo M. J., 1909, vi, 305.
[5] Tr. Am. Surg. Ass., 1909.
[6] Month. Homœop. Rev., Lond.
[7] Am. Med. Mag., 1897, 608.
[8] Tr. Coll. Phys., Phila., 1913, xxxv, 154.

tetanic symptoms eleven days after operation. Death.

CASE 2. Inguinal herniotomy, secondary hæmorrhage. Onset of tetanus within nine days. Death.

CASE 3. Cholecystostomy. Onset of tetanus in 15 days. Death.

CASE 4. Cholecystostomy with drainage. This patient was carefully prepared by two doses of cathartic and enemata and had no diet but tea and toast for three days before operation. Onset of tetanus seven days after operation. Death.

CASE 5. Bilateral inguinal herniotomy. No adherence of gut within sacs which were of direct type. The patient was in the hospital three days before operation with usual pre-operative emptying of the alimentary tract. On the day after operation the patient had a tap water enema. He had no bowel movement for four days after operation. Drank milk freely, made a complete recovery and left hospital 12 days after operation. Six days later, 18 days after operation, he returned with abdominal cramps and stiff neck. Trismus developed. A small pus pocket was found in the left inguinal region, smear of which showed staphylocci only. Recovery after vigorous antitoxin treatment.

CASE 6. Left-sided inguinal herniotomy. Operated on day after admission, usual preparation for operative cases. Eleven days after operation the patient had abdominal cramps, shortness of breath, and pain in the throat. Convulsions followed within a few hours involving the muscles of the trunk, neck and diaphragm. Death. At the autopsy there were found suppurating adhesions of the sigmoid to the deep part of the herniotomy wound, the skin opening and external oblique fascia having healed cleanly. The deeper muscles and tissues in the wound were grayish and infiltrated with a dirty, gray exudate. One of the deep stitches used in the herniotomy passed through the peritoneal coat and wall of the sigmoid, but the mucosa was intact. Smears and cultures were made of the exudate and tetanus organisms were found. Cultures and animal inoculations made from the sutures not entering the bowel wall were negative for tetanus.

Although Matas' idea as to the source and method of infection of post-operative cases in the regions exposed to fæcal contamination is probably correct, I feel that there is more to be said in regard to the retention of the tetanus organisms in the alimentary tract. Some of the cases briefly outlined above and others in the literature developed post-operative tetanus after periods of abstinence from diet which could be contaminated with tetanus and after thorough catharsis which would have emptied the bowel of previously eaten green vegetables, etc. In view of the various experimental and bacteriological data mentioned in the biologic considerations, it seems possible that some human beings carry and excrete tetanus organisms for long periods and are really *tetanus carriers*. Their greatest danger is to themselves because after operative procedures which permit fæcal contamination of the wound tetanus may be inaugurated. This is particularly true of abdominal operations where the gut is bruised or roughly handled and opportunity for tetanus development ensues in accordance with the pathologic requirements. The possibility of hæmatogenous infection must also be weighed. Considering the great number of anorectal, gynecologic, and intestinal operations and the few post-operative cases of tetanus resulting therefrom, it seems that we may attribute those few which are constantly occurring in spite of pre-operative preparation to tetanus carriers.

ANTHRAX

With Report of Cases[1]

By J. S. ULLMAN, M.D., Natchez, Mississippi

A REVIEW of the available literature reveals such a paucity of cases of anthrax in the human race that these are herewith presented. Because such cases are seldom seen in this country, and because it behooves the surgeon to be constantly on his guard lest they may be unwittingly admitted to his wards, it may be well to consider, briefly, the disease itself before taking up the history of these cases.

Anthrax (charbon, malignant pustule, splenic fever, woolsorters' disease, milzbrand) may be defined as "a specific disease caused by the bacillus anthracis, usually communicated from the domestic animals to man, and characterized by a specific lesion at the site of inoculation in the skin by œdematous swelling and lymphatic inflammation, or by intestinal or pulmonary lesions, with general infection, splenic enlargement, grave constitutional symptoms, and high mortality" (1 and 2).

ETIOLOGY

Prior to the discovery of the bacillus many theories as to the cause of the disease were advanced. For instance, Keen (1) quotes Heusinger as declaring anthrax to be "a malarial neurosis dependent upon conditions of climate and soil"!

The bacillus anthracis was the first pathogenic bacterium discovered, and the work of Koch, Pasteur, Klebs, and others has made it probably the best known of all pathogenic micro-organisms. Osler (3) states that "geographically and zoologically anthrax is the most widespread of all infectious diseases."

The organism is rod-shaped (being from 5 to 20 microns by 1 to 1.25 microns in size) with square ends. It stains easily, grows rapidly, and produces highly resistant spores and long threads in culture. It is interesting to note that at a temperature below 18 C. and above 42 C. spores are not produced. The cultures grown at the higher temperatures lose their spore-producing properties, and even upon reinoculation into animals this power is not regained. This fact is taken advantage of in the production of anthrax vaccine.

The disease is transmitted to man only from the infected animal, by handling the animal or its excreta; or it is transmitted from the hides, hair, or other portions of the carcass. "It results always from infection either through the skin or intestines, or in rare instances through the lungs" (3).

In the lower animals it may be conveyed by the bite or sting of insects, or by feeding upon infected carcasses, but most often it is conveyed from grazing in infected pastures. It has been shown that pastures long free from infection may be contaminated by material brought upon the land by overflowing streams. This probably is the manner in which the epidemic, reported below, started. Pasteur was able to show that earthworms working above graves of infected carcasses would bring the bacillus to the surface, where it would be deposited in their excreta.

Males are affected, according to Legge (1), in 96 per cent of cases. The point of infection is most frequently located upon the fingers, hands, forearm, face, head, and neck.

PATHOLOGY

The pathological changes are not constant, but the muscles are usually darkened and may be hæmorrhagic. Ecchymoses may occur, beneath serous surfaces, of all portions of the body. The spleen is enlarged much more frequently in the lower animals than in man. The liver may, or may not, be involved.

The "malignant pustule" is really not a pustule, since bacillus anthracis is not a pyogenic organism. Pus, if present, occurs when the necrotic portions begin to slough,

[1] Read before the Homochitto Valley Medical Society, Natchez, Miss., October 13, 1915.

and only then when a mixed infection is present.

The following description gives such a typical picture of the lesion that it may be well to quote it in its entirety:

Usually there is localized burning and itching at the seat of infection which is generally thought to be due to the bite of an insect, such as the flea, for the spot closely resembles such a bite. After a period of incubation lasting from a few hours to three days (rarely longer) the local symptoms suddenly change. The second stage, that of eruption, now ensues, in which a small papule is seen at the seat of the previous irritation. This rapidly increases in height, and in circumference, and generally presents a spot of dark discoloration at its summit. The itching and burning increase, and within a few hours a vesicle appears at the seat of discoloration in the papule. The vesicle now rests upon an indurated base, and contains a small amount of a serous, frequently bloody, fluid. In the earliest stage, the bacilli of anthrax are present in the central point, but as these tissues become necrotic, the bacilli approach the confines of the lesion, where they are present in great numbers, and from here they invade the tissues in the vicinity, find their way into the lymphatics and lymph-glands. Eventually they gain entrance to the circulation and are distributed by the blood over the system. Bacterial embolism is common. The surrounding skin swells so as to form a slight elevation around the vesicle, which now exhibits the peculiar appearances to which it owes its name of "malignant pustule," although this is not an accurate definition of the pathological condition at the seat of the local disease. The vesicle soon ruptures spontaneously, or is ruptured by the scratching of the patient, and reveals a dark red base, which quickly dries, forming a livid or brownish crust. This is the commencement of the central gangrene or necrosis of tissue commonly observed in the carbuncle of anthrax. The crust becomes gradually larger, until it sometimes reaches a diameter of from one to three centimeters, and the swelling and tension of the surrounding skin become more extensive. A line of new-formed vesicles develops around the margin of the crust, and these vesicles contain a yellowish or brown fluid content.

The crust now gradually becomes free from pain and tenderness, and a doughy or boggy infiltration is felt for some distance in the tissues around the primary sore. The local condition, however, has no diagnostic value as an indication of the infection of the general system (4).

SYMPTOMS

Probably the first symptom noticed is the irritable, burning point at the site of infection. The redness at this point spreads; at the same time the swelling increases. There may be also red lines under the skin radiating away from the point of infection and the spot becomes increasingly tender.

The patient complains of weakness, malaise, rarely more than chilliness, though there may be a moderate rigor, headache, and occasionally vomiting.

If the infection is located in the stomach, obstinate vomiting will very likely be present. In the intestinal type, persistent diarrhœa is a marked feature. The pulmonary type gives the symptoms of pneumonia, frequently with cyanosis and collapse. Brain symptoms such as coma or convulsions may be present in any of the above-mentioned types though usually the patient remains conscious throughout the attack. The febrile curve is not unlike that of other acute infectious diseases — usually ranging from 102° to 105° F.

As the disease progresses the pulse rate gradually quickens, while if the patient lives several days, the temperature may drop to an extremely low level before death occurs (in one of our cases, below 94° F.). As the disease progresses the œdema increases and spreads away from the point of infection.

DIAGNOSIS

The occupation of the patient is significant. The condition should be differentiated from furuncle, carbuncle, erysipelas, and malignant œdema. The furuncle is conical, does not form vesicles, and its areola is not œdematous. The slough is not dry, or dark in color. In erysipelas the sharply defined edges of inflammation, the higher fever in the beginning, and earlier prostration will usually differentiate the two. In malignant œdema there is the definite history of injury, marked pain, rapidly spreading gangrene, and emphysema terminating in 24 to 48 hours.

Of course the smears or cultures from the point of infection will show the bacillus anthracis and clear up all doubt.

In some instances before we are able to obtain the organisms, the diagnosis is possible by means of the Ascoli reaction (4) by precipitin. The "ring formation," a peculiar cloudiness, appears promptly and distinctly by employment of the extractive substances from the spleen. This method makes it

possible to prove the precipitinogen of anthrax not only in the fresh filtrates of visceral organs, but also in material which has been preserved on ice for more than three months. The extractive may be prepared in physiologic salt solution, distilled water, or even ordinary tap water. It is stated that putrefaction of the extractive does not interfere with the test. The suspected material is boiled in an acidulated physiological salt solution (acetic acid, 1:1000) for a few minutes, filtered through asbestos, and the *clear* filtrate is examined by floating it on a layer of precipitating serum, after which it is compared with a control tube containing normal serum. This method has been in use in several veterinary high schools of Italy and has been employed by individual workers elsewhere.

PROGNOSIS

The prognosis is always grave, but less so in the external infection. The pulmonary type gives the highest mortality rate, stated by different observers as ranging from 50 per cent to 75 per cent.

Where the infection attacks the extremities the prognosis is more favorable than where the infection is about the head and neck. Mixed infection, with its attending dangers of pyæmia or septicæmia, increases the gravity of the situation.

TREATMENT

In taking up the treatment the prophylaxis is of the utmost importance. All discharges from the animal or patient should be thoroughly disinfected and burned. The body of animals or human beings dying of this disease should be covered by wrappings soaked in an efficient disinfectant and burned. No post-mortem examination should be allowed. Flies, mosquitoes, and other insects have been shown to convey the infection and should therefore be guarded against. It has been shown by Osler that the ordinary processes of tanning do not affect the spores. Animals may be protected from infection by vaccinating with attenuated, non-spore-forming cultures. Every farmer is familiar with this method.

The curative treatment is admitted by all to be essentially surgical. Wide incision at the point of infection with efficient drainage, and hot, moist, antiseptic applications, if instituted early, offer the greatest hope of recovery.

Of course all sorts of medication have been tried. Some propose emesis and purgation in order to free the alimentary canal from as many bacilli as possible. Others hope to obtain the same results by the use of quinine (in doses of from 15 to 60 grains per day) or by combining quinine and carbolic acid; or the use of a solution of iodine and potassium iodide internally.

Injections of a 5 per cent solution of carbolic acid into the tissues at the outer edges of the œdematous area are claimed to be of value.

Probably the administration of Sclavo's serum offers more hope than any other agent. Sclavo states that he relies upon this alone. In a large number of cutaneous cases his mortality rate was only 6.09 per cent as compared with 24.1 per cent for all cases in Italy.

Sclavo recommends the use of doses of 40 ccm. divided into four parts; but Bandi (quoted by Keen) has used as much as 150 ccm. Bandi contends that the method of Sclavo fails because there is not a sufficient quantity of the antitoxin to neutralize the virulence of the poisons of the disease. Kept cool in a dark place the serum remains fully active for at least two years.

Bouchard and Carrhin claim that the toxin of bacillus pyocyaneus has a curative effect in anthrax. The injection of this toxin, or the use of the carbolic injections, should be undertaken if the serum cannot be had.

The cases herewith reported are interesting in many ways. They occurred on a plantation where there had been no charbon for twenty years past, to a certainty, and possibly longer.

The pasture of which we are about to speak is outside of the levee and, of course, has been overflowed repeatedly. This is probably the most likely method by which the land became infected. We must bear in mind, however, that the infection may have been brought by buzzards, or perhaps by a stray animal.

Last June every animal on the place was vaccinated against charbon, excepting one cow, which escaped the negroes that were driving the animals up. On September 9, 1915, this cow was found dead on the range. There being nothing about the external appearance of the animal to indicate that she had died of charbon, the carcass was ordered skinned.

On September 11 one of those who had helped to skin the carcass, Frank Williams, colored, aged 15, became ill, and it was noticed that his feet were swollen (but after the 15th the entire left side of the trunk became swollen); he had high fever all the time, though about the 15th his skin became cold and clammy; there was nausea and vomiting after this date and the urine was scanty and red. The mind remained clear until the end which occurred on the 17. (This negro died without having consulted a physician, and the above history was obtained from his mother by Dr. M. C. Reeves, Vidalia, Louisiana.)

September 16 Tom Davis (who had skinned the carcass), colored, aged 43, "began to feel bad" and noticed a burning, itching place on his right ankle, but thought he had been "snake-bit" the day before. Continuing to feel bad he consulted Dr. Reeves at his office (September 18, 11 a.m.). His temperature at this time was 102° F. and his pulse 100. There was a small "pustule" on the right ankle, posterior to the internal malleolus. There was a little swelling at this time. September 19, 5 p.m., the temperature was 102° and the pulse 100, while the foot and leg were more swollen than the day before. There was little pain in the leg. The patient, however, complained of pain over the bladder region and micturition was difficult; later in the evening it became necessary to catheterize. There was also a sensation of constriction around the pelvis, which was not relieved by catheterization. The sensations in this region disappeared as the disease progressed. On this date patient began to complain of nausea which continued throughout.

September 20, 8 a.m., the patient was restless, and the temperature and pulse were elevated to 103° and 120, respectively. Upon catheterization only 3 ounces of urine were obtained and this was bloody in appearance. The oppressive pain was described as being higher up on the abdomen. The leg and foot were very œdematous and the lesion was elevated above the surrounding tissues and now consisted of a hard, black crust surrounded by vesicles, around which was a widespread boggy swelling. Hot carbolic compresses were applied and the foot elevated. At 3 p.m., he was again catheterized but only a very small quantity of urine was obtained. The temperature now registered 105° and the pulse 140. The patient was restless and complained of an oppression about the chest. At 5:20 p.m., the temperature had dropped to 102°.

September 21, I saw the patient in consultation with Dr. Reeves. The temperature was 103° and pulse 140; the patient was restless but the urine had become clear. A sample of this urine showed no albumin and no erythrocytes, but granular casts were present.

An incision was made posterior to the internal malleolus down to and including the tendon sheaths which were very tense with œdema. All the tissues were rather pale and had a gelatinous appearance. No pus was found. A drainage tube was inserted in the tendon sheath, and a hot bichloride dressing applied. At 8 p.m., the temperature and pulse were the same, but all other symptoms appeared aggravated.

No serum being at hand, it was decided to employ anthrax vaccine (in the same manner as typhoid vaccine is employed in that disease). Of the veterinary vaccine (No. 1 of the double dosage) 0.1 ccm. was injected without apparent result.

September 22, 6:40 a.m. The temperature was 97° and pulse 150, the skin cold and clammy and the patient much weaker. Saline enemata were given, as well as hypodermics of strychnine and atropine.

As an emergency measure we decided to use serum, and a horse which had been inoculated against anthrax was accordingly bled for that purpose.[1] By 6 p.m., 130 ccm. of serum had been procured and this was given intravenously, and followed by 1000 ccm. of physiological saline containing 0.5 ccm. of digitol. In spite of this treatment and the use of other stimulants, at 9 p.m. the temperature was below 94° and the pulse 160 while the breathing was labored though regular. The patient died at 4 a.m. of the 23d.

Smears and cultures obtained from the wound, the blood, the spleen and the peritoneal fluid all showed anthrax bacilli. The spleen was not enlarged. The tissues were pale and anæmic.

On the afternoon of the 23d two negro men (Robert Thompson, 35 years, and Eddie Bolden, 19 years — who had hauled the hide away) were found to be complaining of headache, pains in the back and knees and were feverish. The older one had had a chill. An injection of 50 ccm. of serum was given intramuscularly to each and repeated the next day. Purgatives were also administered. Within 48 hours both negroes were apparently well again.

We were unable to prove that the last two negroes had anthrax, but we feel that we

[1] Since writing the above paper the following suggestion was made by Dr. E. M. Rank, State Veterinarian, Agricultural College, Mississippi: That a horse be hyperimmunized by giving him 10 ccm. of the second part of the double anthrax vaccine for animals. This dosage will be a safe one and will produce a large quantity of anti-bodies in the horse at the end of about forty-eight hours, at which time the animal should be bled and a serum prepared.

Of course, in the case quoted above the patient's condition did not warrant our waiting so long to prepare a serum.

were doing the safe thing in administering the serum after the experience just mentioned.

The above conclusively shows that the handling of infected material is dangerous in the extreme.

That the serum obtained from an animal immunized by vaccination may, in all probability, be too weak to be of curative value.

That where a regularly standardized serum — such as Sclavo's — cannot be obtained, an emergency serum should be prepared from a recently vaccinated animal, if a competent bacteriologist be on hand to make it.

That such a serum may be of value as a prophylactic agent.

That any serum should be employed in large doses — from 150 ccm. to 250 ccm.— and given intravenously, where possible, and repeated every 6 to 12 hours, if necessary.

I wish to acknowledge my indebtedness to Dr. M. C. Reeves, Vidalia, Louisiana, and to Dr. M. Beekman, Natchez, Mississippi, for the use of notes on these cases; and to the latter is due credit for the idea of making the emergency serum mentioned above.

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2. Bryant and Buck, vol. ii.
3. Osler's Practice, p. 148.
4. Ref. Handbook of Med. Sc., vol. i.

RENORENAL REFLEX PAIN

Report of a Case[1]

By H. A. FOWLER, M.D., F.A.C.S., Washington

PAIN is one of the cardinal symptoms of stone in the kidney. In a typical case, this pain is so characteristic that taken together with the urinary changes, it readily leads to a correct diagnosis. But it requires very little experience to convince one that in many cases of renal calculus the pain is so atypical in character as to be confusing and misleading. Indeed, it may be said that in no other organ of the body is pain so vaiiable as to location, duration, intensity, and irradiation. This is abundantly evident from the statistics dealing with this symptom in a large series of cases. Thus, Braasch in a clinical study of 251 cases of nephrolithiasis states that in only 46 per cent was the pain referred to the affected kidney alone and did it radiate downward along the uieter. Irradiation of the pain was noted as follows: to the gall-bladder in 12 per cent; to the lower abdomen and laterally suggesting appendicitis in 12 per cent; in 22 per cent it was referred to both sides; and in 16 cases or 6 per cent, pain was referred chiefly to the non-affected side. Cabot has shown how frequently other innocent organs have been attacked surgically through an error in diagnosis based upon subjective symptoms alone.

That pain produced by a stone in one kidney may be referred entirely to the kidney of the opposite side was first pointed out by Knowsley Thornton. This assertion was based upon his own operative and autopsy experience. And he concluded that the reason why stones were not found in certain cases where the symptoms were characteristic was that the pain was transferred, and that it was really the healthy, though painful, kidney that had been operated upon.

Guyon, as a result of his clinical investigations, was led to the conclusion that in the pathology of the urinary tract there are three important reflex groups to be considered, and the most important of these reflexes are the renovesical, vesicorenal, and the renorenal reflex. Guyon stated that renorenal reflex pain is common in nephrolithiasis. This form of reflex pain was accepted by Legueu, who called attention to the fact that in some cases, pressure over the painless kidney containing the stone produced, on the contralateral side, the typical pain from which the

[1] Presented in abstract before the American Association of Genito-Urinary Surgeons, White Sulphur Springs, West Virginia, May, 1915.

patient was suffering. The authority for the existence of renorenal reflex pain, therefore, rests in the first place upon the clinical observations of Thornton, Guyon, and Legueu. Henry Morris, on the other hand, denies the existence of this reflex. And the great weight of his authority has been sufficient, apparently, to cause some other observers to question the occurrence of the phenomenon. In view of the contradictory opinions expressed in the literature, which are reflected in the current textbooks of genito-urinary surgery, it seems worth while to review briefly the literature of the subject, to examine into the evidence thus recorded, and to arrive, if possible, at some conclusions justified by such a review.

Before proceeding with this part of the paper I wish to report a case recently under observation which seems to have a distinct bearing upon the question and which stimulated this present inquiry.

On February 27, 1915, I was called in consultation by Dr. Ada Thomas of Washington, D. C., to see a young woman, E. O. H., aged 29, suffering with what appeared to be a typical attack of renal colic. She was lying in bed with a hot water bag applied to the right loin. She was nauseated and had vomited several times earlier in the morning. At the time of our visit the pain which had always been confined to the right side, was not marked, but a few hours before and during the preceding night it had been very severe. The present attack came on a few days before, soon after going to her work at the library in the morning. She was compelled to return home. The pain grew worse and continued during the remainder of the day and the following night. This pain she described as very sharp and severe and was felt in the right loin just beneath the costal border. It did not radiate down along the ureter or in any other direction. Following this attack of acute pain she had been conscious for a few days of a soreness over the region of the right kidney and, as she described it, a deep rumbling pain, was present most of the time.

Being the daughter of a physician she was able to give a very complete and accurate history. At the age of nine years she had scarlet fever which was followed by severe dropsy. This cleared up and she was perfectly well afterward. Menstruation began at fourteen years and has always been regular and normal.

Ten years ago she had an attack of hæmaturia which came on without apparent cause. A day or two later she had a very severe attack of kidney colic. The pain was localized in the region of the right kidney and did not radiate. This attack was associated with nausea and vomiting. The pain lasted only a few hours and the blood gradually disappeared. Following this attack she was perfectly well for the next five years when she had a second attack similar in every detail to the first one. There has been no recurrence of the pain up to the onset of her present illness, but in November, 1914, there was macroscopic blood in the urine. The pain in the former attacks as well as the present one had always been referred to the right kidney. There had never been any pain on the left side and no vesical irritation.

Examination. The patient is a young woman of slight build, apparently in good physical condition except for the pain in the right loin. Examination of the chest was negative. Palpation of the left kidney region elicited no tenderness, muscular rigidity, or pain, local or referred. The right kidney region was tender on palpation, painful, and there was slight muscular rigidity. Abdominal palpation was otherwise negative. The patient remarked during this examination that the tenderness in the right loin and below the costal border was much more marked during the attack of acute pain and that such deep palpation would not have been possible.

The urine, catheterized specimen, was clear, amber, acid normal gravity, and the sediment contained numerous fresh red cells, without pus or infection.

An X-ray examination made by Captain Christy of the Army Medical School showed a distinct shadow opposite the cartilage between the third and fourth lumbar vertebræ on the left side and in a line with the tips of the transverse processes. The right kidney and ureter as well as the left kidney were negative.

Cystoscopy. The bladder was normal. There was no injection of the vessels about either ureteral opening and each side was seen to functionate.

Ureteral catheterization. A wax-tipped catheter was first passed into the bladder for some distance, the cystoscope then being threaded over the catheter and introduced. In this way contact of the waxed tip with the metal instrument was prevented. The catheter was passed 10 cm. into the left ureter and a sufficient amount of urine collected for examination. A No. 7 catheter was passed to the pelvis of the right kidney. After collecting a specimen for chemical and microscopical examination the wax-tipped catheter in the left ureter was advanced slowly until it met an obstruction at a point 24 cm. from the ureteral opening. By rotating the catheter it finally passed the obstruction and advanced easily to the kidney pelvis. The tip of this catheter was then withdrawn below the point of obstruction and again advanced meeting the obstruction which was overcome in the same manner. At the completion of the examination great care was taken to avoid contact of the wax-tipped catheter with the metal of the instrument. Examination of the catheter on removal showed deep spiral grooves cut in the wax, undoubtedly due to a rough stone in the

ureter 24 cm. from its bladder orifice and at a point exactly indicated in the X-ray plate.

Examination of the specimens obtained by the ureter catheter gave the following results.

	Right	Left
Reaction	strong acid	neutral
Albumin	negative	heavy ring
Urea	.016	.002
Microscopic	fresh red cells no leucocytes	red cells, renal cells, leucocytes numerous.

Upon the evidence furnished by the X-ray plate, corroborated by the wax-tipped catheter and the depressed renal function on the left side, the diagnosis of a stone in the *left* ureter was justified although all the symptoms had been referred to the right kidney. From the negative X-ray plate, the ureter catheter, the good renal function, and the absence of pathological elements in the specimen obtained from the right side it was concluded that the right kidney was normal.

Operation. Left ureterolithotomy. Partial closure of the incision into the ureter, cigarette drain, recovery.

The ureter was readily identified and exposed by palpating the stone which was found at the point previously determined. The edges of the wound in ureter were brought together by a simple suture of fine catgut. A cigarette drain was carried down to this point. After the removal of the drain there was a very slight leakage for three days after which the wound was dry and promptly healed. The stone is oblong in shape, gray white in color the surface bristling with sharp pointed crystals with glittering surfaces.

Convalescence was satisfactory and without incident. There has been no recurrence of the pain in the right side up to the present time, eleven months after operation. Examination of a centrifuged specimen of urine six weeks after operation was negative for red cells.

Remarks. Such is the record of our clinical observation. An analysis of this record shows that our patient had a stone in the left ureter situated at a point 24 cm. from the vesical end of the ureter. She had no symptoms whatever at any time referable to the left kidney or ureter. She has had three severe attacks of typical renal colic associated with hæmaturia in which the pain was always localized in the region of the right kidney and did not radiate to the bladder. There had never been any vesical symptoms. The methods of clinical examination employed failed to show any pathological process in the right kidney which might explain the several attacks of pain referred to that side. In fact nothing abnormal was found and we concluded from the result of our examination that the right kidney was normal and healthy. The methods of examination included an X-ray examination of the kidney and ureter, ureteral catheterization to the kidney pelvis, chemical and microscopical examination of the urine obtained by the ureter catheter, and the comparative urea output of the two kidneys during the same period of time. I am not familiar with any further clinical or laboratory methods which might be expected to throw additional light on the question of the possible presence of pathological lesions in the right kidney, of sufficient gravity to serve as a plausible explanation for the pronounced symptoms presented.

In the absence of any demonstrable lesion of the painful kidney and with no other satisfactory explanation to suggest, I believe this to be an example of renorenal reflex pain. I am well aware of the widely different views held by different authorities as to the occurrence of this renoreflex pain. While some authors maintain that renorenal reflex pain must be accepted as a fact, although cases of this kind are extremely rare, others stoutly deny its existence and affirm that in the majority of cases the supposedly healthy kidney is not really sound, that the pain is due to some lesion that has been overlooked. In some instances the lesion may be outside the kidney itself as in the case referred to by Morris.

I am not, however, so much concerned with the existence or non-existence of true renorenal reflex pain. I am more concerned in presenting a clinical observation unique in my own experience and one which I am sure from a perusal of the literature, is unusual. It matters little after all whether we do or do not accept the existence of true renorenal reflex pain. The fact remains that occasionally, though rarely, one may see a patient suffering with typical attacks of renal colic in which the pain is localized in one kidney region and the most careful examination will fail to reveal any lesion of the kidney on the painful side, while a stone is discovered in the opposite kidney or ureter, the removal of which is followed by the disappearance of all symptoms. The important consideration is

that such cases do occur and this fact emphasizes the necessity of making a complete preoperative diagnosis in every case of suspected renal calculus before any surgical interference is undertaken. Such a complete diagnosis involves an examination of both kidneys and both ureters even with the symptoms wholly confined to one side. Had this not been done in the case here reported we would have missed altogether the stone in the left ureter, which, though located on the painless side, was unquestionably producing all the symptoms. It should be further remarked that in all cases of kidney stone the diagnosis can be considered complete only when the exact location of the stone in the kidney or ureter has been accurately determined. The removal of the calculus is thereby greatly simplified, the necessity for an extensive exploration during the operation is avoided, and the trauma resulting from the surgical interference will be reduced to a minimum.

LITERATURE

By renorenal reflex is meant a condition in which the symptoms of disease in one kidney or ureter are referred to the contralateral side, the kidney or ureter of this side being entirely normal, or presenting only slight changes, the character and degree of which offer no plausible explanation for such localization. The symptoms of renorenal reflex are pain and anuria. The underlying cause is almost always calculus disease. In three other conditions tuberculosis, pyonephrosis, and tumor, the phenomenon has been noted. As to the pain, this is completely transferred, and is so entirely confined to the sound side that the patient and surgeon are led into error in supposing the lesion to be on the painful side. The healthy kidney has been operated on for the removal of a suspected stone. As regards anuria the calculus produces complete obstruction of the affected ureter, while the other kidney, although comparatively healthy and the ureter patent and unobstructed, fails to functionate. The anuria may be complete and persist for many days and threaten the patient's life. Pain is, therefore, only one manifestation of renorenal reflex.

As already stated Thornton was the first to establish to his own satisfaction that the symptoms of stone in one kidney may be referred entirely to the kidney of the opposite and healthy side. He records several observations where the diagnosis of stone in one kidney has been made, based upon the clinical symptoms, and operation has revealed a stone in the opposite kidney. The location of the stone in these cases was determined by a preliminary exploratory abdominal incision. In this manner he was able to determine the presence of a stone in the opposite kidney which did not present symptoms. His clinical operative experience was also supported by the records of similar cases coming to autopsy. Thornton suggested that the failure to find a stone in at least some of the cases presenting typical renal colic was due to the phenomenon of transferred pain — the stone was missed by exploring the wrong, though painful, kidney.

The now well-known case of Godlee has often been quoted in support of this view. In the *Practitioner* for 1887, p. 241, Godlee writes as follows: "Mr. Knowlsey Thornton has staggered us with the assertion that all symptoms of stone in one kidney may be caused by the presence of stone in that of the opposite side." He reports the following case:

> A young man, 24 years old, was operated upon by Mr. Beck, the kidney was exposed and needled without results. No stone was found and there was no relief of colic. Later the patient consulted Mr. Godlee on account of pains located on the right side, which were so severe that it seemed best to cut down on the kidney again and incise it. This was done and the kidney thoroughly explored without finding any stone. Blood was passed after the operation, showing that the ureter at all events was not completely blocked, and no urine escaped from the wound. The colic was not relieved. Seven weeks after operation the patient passed a stone *per vias naturales*, and gave credit to Godlee for having dislodged it. Close questioning of the patient brought out that only at times did the pain shoot over to the left side. The patient felt sure that the trouble was in the right kidney. Godlee remarks that of course a stone may have been well down in the ureter on the right side without completely blocking it, or it may have been in the left kidney all the time. A footnote states that since the above report the patient was again confined to bed with left renal colic.

In the light of our present knowledge

skepticism based upon the cases above reported is entirely justified. The evidence presented by the clinical experience of Thornton, Guyon, and Godlee, while highly suggestive, is by no means convincing. The cases as reported will not stand criticism. Morris in his *Surgical Diseases of the Kidney and Ureter*, vol. ii, p. 84, says:

> It is important to know that a stone in the kidney will sometimes excite sympathetic pain and irritation in the other; but, if this is transferred, or if the sympathetic pain is of an aching character, not of a spasmodic or colicy description, it is only occasional, and never occurs except as an accompaniment of severe pain of the affected side. So far as my own experiences and researches go, there is not a single case which affords satisfactory evidence of symptoms on one side only being caused by a stone in the kidney of the other side. The presence of a stone in the painless kidney is not proof that the painful opposite organ is not affected. That the attacks on the painful side have ceased after removing a calculus from the painless kidney is not conclusive; this may be nothing more than a coincidence due either to the accidental shifting of a calculus in the painful kidney, or to the calculus becoming lodged in some immovable manner. There may be very advanced disease of the kidney on the painful side and a symptomless calculus in the opposite kidney. In a case which has been under my care of late there was a sarcomatous growth in the right kidney with hæmaturia, but an entire absence of pain and tumor on the right side throughout the whole course of the disease, yet intense pain was experienced in the left renal region radiating over the left side only. The inference would have been that this was a typical case of renorenal reflex pain had not symptoms during the last few weeks of life and a post-mortem examination shown that the left-sided pain was due to a similar new-growth involving the left transverse processes and the left side of the bodies of the lower dorsal vertebræ. I consider the doctrine of renorenal reflex pain with the absence of pain in the affected kidney as unproved and unsound and if acted upon in practice, likely to lead to very serious and dangerous results.

It must be remembered that this view of Morris represents the preroentgen period, and for that reason does not carry as much weight as it might. If the question as to whether or not renorenal reflex pain ever occurs rests on no more convincing evidence than that furnished by the literature antedating the period of the X-ray, cystoscope, and ureter catheter, I am quite sure that the verdict must be "not proved."

It is interesting in going over the literature to find that many authors accept, as a matter of fact, the existence of renorenal reflex pain, call attention to its frequency in nephrolithiasis, and point out that it may lead one into error in exploring the wrong kidney, but they do not give any illustrative cases from their own experience. Albarran states: "One observes certain patients who suffer on the side opposite the lesion; reflex renorenal. He (Guyon) has demonstrated this in a large number of cases. In certain cases the pain persisting upon the healthy side has led to an error in diagnosis and Godlee was led to do a nephrotomy upon the healthy organ." Legueu says: "There are cases of renal calculus in which the calculus produces subjective disturbances referred to the healthy kidney; this is one of the manifestations of renorenal reflex. In examining by bimanual palpation the kidney containing the calculus one sometimes sees the patient manifest sudden pain on the opposite side. This fact is of great importance as the surgeon may be led into the error of incising the healthy kidney as was done by Godlee."

Israel in his monograph speaks of the occurrence of renorenal reflex pain in the following language: "Ja, es kommt vor dass eine einseitige Steinverstopfung mit einen contralateralen Schmerzanfall beginnt, obwohl die Niere und Ureter der schmerzenden Seite frie von Steinen sind. Dieses von Albarran berichtete Verkommniss veranlasste einen Eingriffen der nicht occludirten Niere, an welcher als ursache der Tauschung nur eine congestiv Schwellung ohne Stein gefunden wurde."

Kapsammer evidently accepted renorenal reflex as a fact. To quote: "The pain can, furthermore, appear in the side opposite to the kidney bearing the stone, and when this kidney is enlarged (compensatory hypertrophy) it may be the one to which the operation is directed as happened in one case of Morris.[1] Moreover, without hypertrophy of the kidney the wrong one may be subjected to surgical attack on account of pain referred to the contralateral side; renorenal reflex pain of the Guyon school."

As a matter of fact the number of cases

[1] Brit. M. J., 1892.

scattered through the literature is small. The more recently reported cases naturally have been much more carefully studied and are, consequently, of greater importance in their bearing upon the question under consideration. The cases I have succeeded in finding are as follows:

David Newman,[1] reporting three additional cases makes the following comment: "In the *Glasgow Medical Journal*,[2] I tried to show that my experiences led me to believe renorenal reflex pain is a fact which must be accepted and in proof of the opinion I cited the following cases; one under the care of Mr. Maylard, a second published by E. Owen, and a third personal case. In addition I have three others which demonstrated beyond a doubt that renorenal reflex is a fact which must be accepted:"

Maylard's Case. Patient aged 38, suffered a nagging pain for six months in the right iliac region. The attacks lasted 24 hours and caused vomiting. He had four attacks of acute iliac pain. Following one of these attacks blood and albumin was found in the urine. He never had had any frequency. The right kidney was explored but no stone was found although a catheter was passed down the ureter. There was suppression and death. Post-mortem examination showed the right kidney previously explored to be healthy and the left to contain a calculus the size of a pea in one of the upper calyces.

Edmund Owen's Case. The pain was limited to the right side. The right kidney was explored with negative results. Later a large phosphatic calculus was removed from the left kidney (400 grams). Owen comments as follows: "I am well aware that it is not a very unusual occurrence for a surgeon to operate upon the wrong kidney in his search for a stone, but I do not think a more conspicuous instance than this of the untrustworthiness of the subjective symptoms of pain in renal calculus is likely to be forthcoming. Subjective signs are proverbially untrustworthy through the whole range of surgery; but in the case of the kidneys, which have drawn their nerves blindfold from the epigastric pool it is small wonder if, in the absence of subjective signs, the patient and surgeon are sometimes led by them to make mistakes."

Newman's Case 1. The patient, a male aged 58 years, has had dull pain in the *left* lumbar region for the past seven years with acute attacks of renal colic at intervals of 2 or 3 months. The attacks came on after exercise and were succeeded by hæmaturia. Cystoscopic examination during the attacks showed blood from the right side only. This was observed on several occasions. Exploration of the right kidney advised but the patient refused as he was convinced the trouble was on the left side.

Newman's Case 2. Female, 25 years old, had suffered *left* renal colic attacks covering a period of 5 years. Cystoscopy showed blood from the right side. An X-ray examination showed a stone shadow in the right pelvis after four futile attempts. Right nephrotomy, recovery, and relief of all symptoms.

Newman's Case 3. History of right renal pain for a period of eighteen months. After several attempts a positive stone shadow was obtained on the left side. Left nephrotomy was done and a stone removed. Recovery and relief of all symptoms followed.

Newman's Case 4. The history of the patient is given in considerable detail. It is particularly interesting that the underlying cause was non-calculus pyonephrosis. The pain was always referred to the left side. Nephrotomy and drainage of the right pyonephrotic sac was followed by a cessation of all pain.

Rumpel[3] reports the following case:

A married woman, aged 35, suffered with an attack of left-sided colic in the sixth month of pregnancy. After the birth of the child hæmaturia occurred, accompanied by a dumb pain in the left side. A diagnosis of tumor of the left kidney was tentatively made. Cryoscopy indicated kidney insufficiency. X-ray examination showed a stone shadow in the *right* kidney. Ureter catheterization gave evidence of nephritis on both sides, more marked on the left. Right nephrolithotomy freed the patient from all pain.

Victor Blum contributed a paper on, "Die Bedeutung der renorenalen Reflexen fuer die Pathologie und Diagnostik der Nierenkrankheiten," which appeared in the *Wiener klinische Wochenschrift*.[4] In this paper Blum reports three personal observations of renorenal reflex pain.

Case 1. Female, age 54, suffered for six years with attacks of renal colic, the pain radiating to the bladder, and accompanied by hæmaturia. These attacks were separated by intervals of weeks or months. The pain was always on the left side. The last attack occurred just before the patient came under observation, accompanied by anuria for several hours, and followed by hæmaturia on exercise.

The left kidney descended, the lower pole at the level of the crista ilii, not painful and not enlarged. The right kidney was palpable below the costal border and on deep inspiration the whole surface could be felt. On deep pressure over the right

[1] Lancet, Lond., 1909, i, 1111.
[2] Vol. liv, 103.
[3] Fortschr. a. d. Geb. d. Roentgenstrahlen, Hamburg, 1904, x, 7. Quoted by Josephson.
[4] 1907, No. 40, 1208.

kidney pain was regularly produced in the left kidney similar to that during the attacks of colic.

Cystoscopy. Cystitis granulosa fundi. Both ureters normal with cloudy, bloody urine escaping from the right side.

Ureteral catheterization. Right — light, turbid, bloody urine, containing albumin; sediment contained numerous red cells, leucocytes, epithelium and granular casts. Left — clear, amber urine, free from albumin; sediment contained few red cells and leucocytes but no kidney elements.

X-ray examination of both kidneys: Left negative; right two stones, one the size of hazelnut, the other the size of a pigeon egg. *Operation:* right retroperitoneal pyelolithotomy. Several months after the operation there was sudden pain in the left kidney region, subsiding with warm applications. Subsequent cystoscopy and X-ray examinations gave negative results. No hæmaturia. Since operation the patient has remained perfectly well.

CASE 2. Female, age 41. Two years before, the patient suffered slight attack of colicky pain in right hypogastric region lasting several hours. For 6 months she had similar attacks on the left side, no hæmaturia, no gravel. The right kidney pole was a hand's breadth below the costal border and was not painful. The urine was cloudy, with a trace of albumin; there were leucocytes, red cells, and hyaline casts.

Cystoscopy showed diffuse cystitis. *Ureteral catheterization:* Right, urine cloudy, alkaline, with trace of albumin: left, clear, acid, albumin negative. X-ray examination: Right, stone shadow size of walnut; left, negative. *Operation*, right posterior pyelotomy.

Subsequent history. At times pain always referred to the left side. Recent X-ray examination and ureter catheterization show normal condition. After lavage of right kidney pelvis with 5 per cent silver nitrate solution all pain disappeared.

CASE 3. Male, age 35, for three years suffered with attacks of kidney colic and hæmaturia referred always to the left side. Cystoscopy showed a calculus the size of a hazelnut in the opening of right ureter. X-ray showed a stone shadow the size of pea in pelvis of the right kidney. Left side was negative. After passage of calculus the patient was absolutely free from pain and would not submit to further surgical interference.

Blum states further, that in addition to nephrolithiasis, there were also cases of unilateral renal tuberculosis and unilateral tumor under observation, in which pain was referred to the opposite kidney which was found healthy. Even after extirpation of the diseased organ the pain remained which could be explained only as renorenal reflex from the kidney stump. By all the methods of clinical examination the kidney in which the pain was located was found to be entirely healthy.

The most recent paper which I have been able to find is one by Josephson.[1] Josephson considered both renorenal reflex pain and reflex anuria. He reports in detail a personal observation of reflex pain which he claims is the most carefully and thoroughly studied case so far recorded.

Female, age 52, gave a history of attacks of abdominal pain dating back sixteen years (1894). Three years after onset she consulted Professor Lennander who made a diagnosis of stone in the right kidney and performed a right nephrotomy without finding a stone. Five weeks later the pains recurred. During one of these attacks, with pain referred to the right side and with an elevation of temperature, appendicitis was suspected, but under observation in the hospital this diagnosis was abandoned and the trouble was considered to be "digestive." During the past several years the attacks of pain have averaged only one or two attacks a year and it is always referred to the right side. Trouble in the left kidney was never suspected as shown by the fact that in 1909 her physician sent her for an X-ray examination of the right kidney only, and this showed only an enlarged and descended kidney. The patient was referred to Josephson for cystoscopy and ureter catheterization.

Cystoscopy: Bladder and ureters normal. *Catheterization:* Right — abundant clear straw urine, no albumin and no sediment. Left—light, turbid urine, albumin strongly positive. Sediment contained pus and blood. An X-ray examination showed three stones in left kidney; right, negative.

Operation: Left nephrectomy. The kidney consisted in a large part of a fibrous sac with little secreting substance. The stone was composed of phosphates with a mixture of calcium carbonate. The patient remained well for a year after operation or up to the time of the report. There was no return of the pain and the quantity and character of the urine remained normal.

Haenisch, quoted by Josephson, reports four cases with symptoms on one side and a stone shadow in the opposite kidney. In only one case was the diagnosis confirmed by operation and relief of all pain. Similar cases are reported by Forssell.

We know perfectly well that the pain produced by a stone in one kidney may radiate to the opposite side. This is commonly observed. It is also stated in the literature on nephrolithiasis that such pain is commonly referred entirely to the other side. This we believe is, on the contrary, far from being commonly observed. But that such complete transference of pain does occur, true

[1] Ueber den reno-renalen Reflex. Nord. med. Ark., 1911, xliv, No. 17.

renorenal reflex pain, I believe we must admit from the evidence furnished by the observations recorded. While the earlier reported cases are open to criticism on the ground of incompleteness, according to the requirement of our present standards and methods of investigation, this objection cannot be applied, for example, to the observation of Josephson, Blum, Newman, Maylard, Owen, and the case above recorded. It may be added further that such a careful observer as Thompson Walker, without detailing his observations, sums up his experience as follows: "The most important reflex pain is that in which pain is referred to the second kidney (renorenal reflex). I have seen two cases where the referred pain was present without pain in the kidney containing the calculus, and there are a few similar cases on record."

From my own experience and a study of the literature, I believe the following conclusions are justified and well founded.

1. The symptom of pain arising from disease in one kidney may be referred entirely and completely to the opposite side, the latter organ being healthy so far as we are able to ascertain by our present methods of examination. In the absence of any demonstrable lesion either within or outside of the kidney sufficient to account for such localization of symptoms we are justified in assuming the pain to be reflex — renorenal reflex pain.

2. Cases of renorenal reflex pain are rare. Only a relatively small number have been reported in detail.

3. The importance of this phenomenon, from the standpoint of diagnosis, is not as great as it once was. Errors in diagnosis are not so apt to occur from misleading subjective symptoms since the employment of more accurate means of examination, X-ray, cystoscopy, ureter catheterization, and renal functional tests has become more general. The occurrence of this phenomenon, however, emphasizes the importance of a thorough and complete pre-operative examination of every case of suspected renal calculus.

THE THYMUS AND ITS TUMORS

Report of Three Cases of Thymoma

By JAMES EWING, M.D., New York

NO group of tumors has more successfully resisted attempts at interpretation and classification than those of the thymus. The problems involved include those which have complicated the embryological and histological study of the gland, and added difficulties arise from the comparative rarity and considerable diversity of the tumors and from the somewhat imperfect knowledge of the general pathology of the thymus.

A short résumé of the knowledge of the origin and structure of the gland will facilitate the interpretation of its tumors (Hammar).

ANATOMY

The thymus is a paired organ arising from evaginations of the third branchial clefts (Thymus III). Its anlage is contiguous with that of the parathyroids arising from the same clefts, a relation which explains the occasional presence of parathyroid alveoli in the thymus, as well as the rare association of thymus tissue with parathyroid in the thyroid gland. A second portion of the thymus arises from the fourth cleft where it holds the same relation to the parathyroid developed from this cleft (Thymus IV). From these four sources the growing entodermal epithelium coalesces to form a four-lobed fœtal organ, which with the descent of the heart becomes drawn out in an elongated double pear shape. In Hammar's early fœtal models the stems stretch from the lateral lobes of the thyroid down below the sternal notch where the main mass of the gland develops, the stems disappearing. This mode of origin only partly explains the occurrence of acces-

sory thymus lobes beside and below the thyroid (Erdheim) and laterally in the neck. Sharp describes a large accessory thymus extending from the anterior border of the trapezius behind the sternomastoid and clavicle.

The fully developed organ consists of a stroma and reticulum, parenchyma, and capsule. The supporting stroma is chiefly found in the network of arterioles, capillaries, and venules to which is confined practically all of the connective tissue within the organ. The finer stroma is a derivative of the original epithelium of the gland which becomes elongated into a fine reticulum in the meshes of which lie the parenchyma cells. This reticulum has nodal thickenings or syncytia, and may be stretched into fine fibrils. By accumulation of its cells in the medulla are formed concentric groups of flat cells (Hassall's corpuscles) with which the reticulum is directly continuous, while on the periphery in many fœtal glands the epithelium appears in groups and cords in cubical or cylindrical form. Hassall's corpuscles are therefore not remnants of fœtal epithelium but collections of adult reticulum cells. In the medulla the reticulum is far more abundant than in the cortex.

The parenchyma cells have the appearance of small lymphocytes from which they have not been successfully distinguished by many studies directed to their morphology, microchemical reactions, serological relations, or behavior in most pathological conditions. Their origin is as yet undetermined. In favor of the view that they are epithelial derivatives as claimed by Beard, Stohr, and others, the following facts may be cited. (1) The occurrence of transition forms between the reticulum and the lymphocytes (Prenant, Bell). Yet Maximow is able to distinguish between the small darkly-staining epithelium and the lymphocytes. (2) The very early appearance of lymphocytes in the thymus. (3) The apparent absence of any signs of infiltration by lymphocytes from without. (4) The apparent transformation of small thymus-cells into epithelium. Against the epithelial origin stand chiefly the evident identity of the cells with other lymphocytes, the development of other lymphoid organs by the inwandering of lymphocytes, and the behavior of these cells in pathological conditions. Most observers, including Maximow, Hammar, and Wiesel, consider the thymus an organ with peculiar reticulum of epithelial origin infiltrated by lymphocytes. Yet the organ never assumes either in structure or functions the position of a simple lymphoid organ. In many conditions it fails to participate with other lymphoid organs in systemic diseases (Hart).

In addition to the lymphocytes other cells are often seen in the thymus. Shaeffer observed many plasma cells derived from the lymphocytes in the involuting gland, and with these may occur eosinophile cells and mast cells (Maximow). Watney describes giant phagocytes. Myoid cells with cross striation are scanty but very constant derivatives of the epithelium. Wasutatschkin, however, considers that they are derived from the muscle-cells in the capsule. The formation of red cells appears to be limited to lower animals but evidences of the formation of leucocytes are frequently observed in man.

The efforts to establish the thymus as a gland of internal secretion and a unit in the chromoffine system are reviewed by Wiesel.

GENERAL PATHOLOGY

A horn of thymus tissue reaches upward to the thyroid gland in 20 per cent of young subjects (Rieffel), and strands of thymus-tissue may encircle the great vessels of the neck and the vagus nerve at the level of the hyoid bone in the infant (Harman, Bien). Accessory lobes appear occasionally in the thyroid and in connection with the parathyroids.

The weight of the thymus at birth varies greatly, from 2 to 14 grams, but averages about 7.7 grams (Bovaird and Nicoll). It increases in size at least to the fifteenth year when the average weight is from 20 to 28 grams (v. Sury, Ronconi). It then steadily diminishes but persists in most subjects throughout life. Its proportion to the body weight is highest at birth, 42 per cent, but after 25 years the permanent ratio of 3 per cent is reached. Owing to numerous

accidental variations it is extremely difficult to establish the existence of a hypertrophy unless of very marked degree. Involution takes the form chiefly of fat invasion of the parenchyma with persistence of many Hassall corpuscles. Simple hypertrophy of the thymus occurs in infants in which the enlarged gland exerts, at least in part, a mechanical effect in fatal thymic asthma by compression of the trachea. The structure of these glands is usually normal. In status lymphaticus the thymus usually exceeds the normal weights for the age and weight of the patient, and at times the excess is very marked. In Graves' disease, thymus hypertrophy is nearly constant and often marked. In all of these conditions the hypertrophy is due to lymphocytic hyperplasia, and does not reach the grade of a neoplasm. In aberrant thymus tissue the hyperplasia has at times been very active as in Sharp's lymphadenoma of a cervical thymus. Hyperplasias interpreted as lymphadenomata are described by Rolleston, Edmunds and McKenzie, Pepper and Stengel, and Hektoen. In these cases the organ was several times the normal size, the capsule was intact, the medulla largely obliterated, and Hassall's corpuscles widely scattered. Tarozzi described as simple hyperplasia a very large encapsulated tumor occupying all the anterior mediastinum in a boy of 18 years.

Proliferation or more correctly increase in number of Hassall's corpuscles occurs in Graves' disease (Soupault) and in hæmophilia (Acland).

Exfoliation of very numerous large reticulum cells in the involuting thymus has been described by Lochte in gangrenous gingivitis and in leukæmia. The thymus is said to participate with other lymphoid organs in the changes of leukæmia, pseudoleukæmia and granuloma malignum, but Schridde failed to find any changes in this organ in leukæmia and pseudoleukæmia. Hahn and Thomas collected several cases of thymic tuberculosis.

Cysts form in the thymus from several sources (Pigache, Beclere, Hueter).

1. The epithelial canals of the embryonal thymus may persist and form one or several small or large cysts in or along the horns of the gland. They are especially frequent in syphilitic infants. Each lobe of the organ may be converted into a large cyst (Bednar). Pollosson and Piery describe a congenital multilocular cyst of a cervical thymus extending from behind the sternum to the mid-carotid region. It was lined by flat pavement cells. In a sclerosed and luetic thymus in a man of 25 years. Hueter found general cystic alterations. The cysts were lined by flattened cells, filled with mucoid and lipoid material, and into many of them grew polypoid masses of thymus tissue. The origin was attributed to persistent epithelial cell groups. Westernak recognized a mediastinal cyst lined by ciliated epithelium by means of thymus tissue in the wall, and he attributed its origin to the thymus duct. The demonstration of lymphoid tissue and Hassall's corpuscles in the wall aided Funke in the recognition of a thymus cyst in the thyroid.

In Graves' disease Soupault describes multiple cysts lined by columnar epithelium. In a man of 69 years he found a thymus 15cm. in length, hyperplastic above, but in the lower half a diffuse overgrowth of epithelial cells and small cysts filled with mucus.

2. Dermoid cysts, of which Hare has collected nine cases, may arise from portions of the ventral ectoderm, or from the branchial clefts. Rolleston described a compound cyst with adenomatous structures resembling Lieberkuhn's follicles and areas of cartilage and sarcoma.

3. Invasion and distention of Hassall's corpuscles by lymphocytes is of common occurrence and many small cysts may form throughout the gland by degeneration of these wandering cells. Chiari showed that Dubois' abscesses consist of distended corpuscles filled with lymphocytes. The lining of these corpuscle cysts is of cubical or flat epithelium. All these cysts are regarded by Ribbert as derived from persistent embryonal tubules.

4. Cystic lymphangioma is described by Seidel in an infant of 2½ years. The entire organ was the seat of many small cysts filled with fluid blood and lined by flat endothelial cells.

PRIMARY TUMORS OF THE THYMUS

Primary tumors of the thymus are probably not as rare as the scanty reports would indicate. Rubaschow collected 69 cases but questioned the thymic origin of many. The age of incidence of 33 sarcomata was: before 25 years, 18 cases; from 25 to 40 years, 8 cases; more than 40 years, 7 cases. Carcinomata occur in later years and usually after 50. Steudener found a large lymphosarcoma in an infant of one year. While Virchow believed that thymic hypertrophy led to tumor growth, Bartel's statistics do not show that cases of status lymphaticus are especially prone to develop thymic tumors. Eisenstadt's case gave a history of trauma. The age of incidence and the usual course of involution strongly suggest that thymic carcinoma is affected by disturbances in the natural process of involution.

The origin of sarcomata seems closely connected with that of other lymphosarcomata and not a few of these cases show marked resemblance to, or practical identity with, granuloma malignum. Analogy suggests that the peculiar reticulum cells of the thymus may at times respond to infection by inflammatory and eventually neoplastic overgrowth.

CLASSIFICATION

Thymic tumors fall into two main groups: (1) Lymphosarcoma or thymoma, composed of a diffuse growth of round, polyhedral, and giant cells. The chief source of this tumor is probably the reticulum cell, but lymphocytes are often present in abundance, and (2) carcinoma arising from the reticulum cells. To these may be added very rare and somewhat questionable cases of tumors attributed to the stroma and called (3) spindle-cell sarcoma or myxosarcoma.

Owing to the uncertainty which still surrounds the nature of the thymic round cells the term "thymoma" has been suggested by Thiroloix and Debret, Simmonds, and others, for tumors of this origin, while Schridde employs the phrase "malignant thymus tumors."

The exact origin of the so-called lymphosarcomata of the thymus remains undetermined. My own study of several cases has led to the conclusion that the thymic round-cell tumors differ from other round-cell tumors of lymph-nodes, that the reticulum cell is here the chief or sole source of the tumor the lymphocytes being largely passive, that these tumors form a malignant subdivision of granuloma malignum. If these conclusions are correct the term thymoma deserves recognition.

1. *Lymphosarcoma*, or thymoma is the most frequent form of thymus tumor. The tumors occupy the anterior mediastinum in the position of the thymus, and usually extends from the sternal notch as high as the thyroid down to the diaphragm. Many authors have questioned the diagnosis of thymic origin based on the location of the tumor but the objections seem to apply chiefly to clinical diagnosis. There is little difficulty in distinguishing thymic tumors at autopsy from tumors of mediastinal lymph-nodes, lung or sternum. They usually surround and compress the trachea, bronchi, pericardium, and great vessels. Both by compression and less often by invasion of vessels and passages they cause death by asphyxia and venous obstruction which may increase gradually or supervene suddenly. The more rapidly growing tumors may be soft but as a rule they are found to be remarkably dense from diffuse fibrosis. The soft tumors may be vascular and hæmorrhagic while the firm growths exhibit a characteristic lobulation from dense fibrous septa. Rarely areas of softening and cyst formation are observed. In many cases the tumors exhibit a characteristic creamy yellow or lemon color.

A strict encapsulation within the mediastinum has been a notable feature in some histologically malignant growths, but the more malignant forms regularly become adherent to surrounding organs, and invade pleura, lung, pericardium, walls or lumina of vessels, and trachea. The bronchial and cervical nodes are frequently invaded. The axillary nodes may be enlarged and in Gabcke's case the invasion of nodes was very widespread. Occasionally there are metastases in the organs, spleen, liver, adrenal, pancreas, and kidney (Zniniewicz). Perforation of the

chest-wall has occurred in several cases and was the first localizing symptom in a case I have recently observed (Seebohm, Zniniewicz, Le Tulle). Fracture of the humerus from bone-marrow metastases is recorded by Zniniewicz, and infiltration of the orbits, brain and other organs, by Meigs and de Schweinitz.

The structure of these tumors varies greatly. Exactly the same difficulties are encountered in their histological classification as one meets with tumors of lymph-nodes. In one group the structure resembles that of an infectious granuloma of the type of Hodgkin's disease. The tissue presents lymphocytes, plasma cells and larger polyhedral cells, irregularly distributed. Several cases of this type have been recorded with emphasis on the presence of many large polyhedral or giant cells (Ertmann, Weigert and Laquer). These large cells must be derived from the reticulum. When they become very numerous the lymphocytes largely disappear and the tumor may be classed as a carcinoma, as has commonly been done by French writers (Le Tulle). In another group the reticulum cells are said to be missing and the tumor is composed of a diffuse growth of small round cells (Le Tulle Stockert). These tumors have not been distinguished from other lymphosarcomata, but it does not appear that any definite effort has been made to do so. The existence of a pure lymphocytoma of the thymus apart from leukæmia does not appear to have been established. The blood-vessels may be very numerous and in some cases cells of medium size may form sheaths about the vessels. When the perivascular arrangement becomes very marked and lymphocytes are scanty, the diagnosis of endothelioma or perithelioma may be suggested as in the cases of Hahn and Thomas and Mandelbaum and Celler. It seems highly probable that these cells arise from the reticulum producing an analogue of perivascular endothelioma of the lymph-nodes.

In the same manner may be explained the mixed tumors described by Gabcke and Schneider, who found round and spindle and many giant cells in their tumors, all of which may readily be derived from the reticulum.

On close analysis the round-cell tumors of the thymus are found to differ in structure from the round-cell tumors of lymph-nodes. The lymphocytes are scanty. The chief cell showing mitosis is often polyhedral, with acidophile cytoplasm, vesicular nucleus and well developed nucleioli. They often cling to the walls of numerous small capillaries where they assume a cubical or even cylindrical form. They frequently produce abortive Hassall corpuscles. The giant cells are of two main types: (1) pale staining reticulum cells with irregular outlines distended with vacuolas and red cell detritus; and (2) myeloid giant cells with opaque acidophile cytoplasm and many vesicular nuclei. These giant cells differ from the smaller giant cells of lymphatic Hodgkin's disease. The marked fibrosis suggests the desmoplastic property of carcinoma.

2. *Thymic carcinoma.* In many cases the main tumor-cell appears in the form of pavement, cubical, or rarely cylindrical epithelium and the growth must be classed as carcinoma.

The gross anatomy of thymic carcinoma is identical with that of the hard thymomata of round-cell type. Although metastases may occur, it is notable that the invasion of surrounding organs is less active than is usual with a distinctly carcinomatous tumor. An aberrant thymic carcinoma containing lymphoid tissue and numerous bodies resembling Hassall's corpuscles was observed in the thyroid by Achard and Paisseau.

The structure in typical cases presents coherent sheets, cords and columns of large, flat, or polyhedral cells, lying in dense connective tissue. Hornification is absent, but concentric layers of flat cells may form structures resembling Hassall's corpuscles (Thiroloix, Debret; Paviot, Gerest). In other cases the pavement characters are less evident and the cells are chiefly cubical and form alveoli. Le Tulle and Ambrosini found accumulations of mucus in the spaces of an alveolar carcinoma. In many cases both round cells and epithelium participate in the tumor process and the authors speak of the growth as carcinosarcoma or adenosarcoma. Thus in Rubaschow's case the main mass was composed of round cells in which lay many foci

of flat epithelium forming pearls or surrounding blood-vessels. Giant cells of a variety of forms are frequently present.

3. *Thymic sarcoma.* Although it has been commonly assumed that various spindle-cell or alveolar or perivascular tumors arise from the connective-tissue stroma of the thymus, this origin has never been fully traced and there are strong grounds for concluding that all the so-called spindle-cell sarcomata and endotheliomata are varieties of thymoma. Congenital myxoma, 10 x 18 cm. in dimensions, weighing 182 gr., containing lymphocytes and Hassall corpuscles in the tumor-tissue was observed by Caso in an infant of 2½ months, and a similar case is described by Winogradoff.

Interpretation of thymomata. The foregoing review of the structure of thymus tumors reveals extreme confusion in the nomenclature employed by different authors, great difficulty in establishing sharply defined varieties, and the existence of transitional forms connecting the two types. The great polymorphism of the cells noted by Ambrosini has been emphasized by later writers as the chief characteristic of thymic neoplasms and has led to the use of the term thymoma. It is significant that the carcinomata have been recorded almost entirely by French observers while practically all the German reports are of sarcoma. Yet Le Tulle and Ambrosini describe as carcinoma, tumors which have many of the features which Ertmann and Zniniewicz have designated as sarcoma. It is also clear as in Dansac's, Hauser's and Rubaschow's cases that many tumors present an overgrowth of both reticulum and parenchyma cells. A full survey of the structural variations reveals at one extreme a mixed process involving lymphocytes and reticulum cells, with giant, plasma, and eosinophile cells producing a structure nearly identical with Hodgkin's granuloma. At the other extreme are nearly pure tumors of rounded or epithelial reticulum cells; i.e., lymphosarcoma and carcinoma. Exactly similar relations exist between tumors of lymph-nodes, including Hodgkin's granuloma and the "sarcomata" arising from it, pseudoleukæmia, and pure endothelioma. Hence the conclusion is reached that the great majority of thymus tumors and especially the mixed growths represent infectious granulomata or particular forms of cell overgrowths arising on the basis of an infectious granuloma. Detailed evidence supporting this conclusion is presented in the writer's study of endothelioma of lymph-nodes. This etiological point of view offers a simple explanation of the great variety of structural forms which thymus tumors present.

In a series of cases of Hodgkin's granuloma the granulomatous process has shown malignant properties both in local aggressiveness and in the production of metastases. Such cases are recorded by Yamasaki, Chiari, J. E. Welch, Symmers, Karsner, and Beitzke. In most of these cases it is stated that the main tumor was mediastinal and occupied the region of the thymus, while the structure presented a diffuse growth of cells larger than lymphocytes and many giant cells of myeloid type. In the report of Symmers' case, studied in this laboratory, a thymic origin was suggested. I have re-examined various portions of this tumor and find in it all the features of thymoma including Hassall's corpuscles, polyhedral reticulum cells, and myeloid giant cells. In the light of this and other cases it seems highly probable that the mediastinal Hodgkin's disease of the above writers is a thymic tumor which should be separated from other forms of Hodgkin's disease, and owes its malignancy to its origin from peculiar reticulum cells of the thymus.

CLINICAL COURSE

Many thymus tumors are highly malignant and prove rapidly fatal from asphyxia, but the actual duration is difficult to determine. Ambrosini's five cases were all fatal in from two to nine months. The very rapidly growing tumors are usually very cellular and vascular. In one of Zniniewicz's cases lasting ten weeks there were general metastases, while in Ambrosini's case of two months' duration the extensions were local, and Erttmann's tumor of two months course was vascular, contained very long polyhedral cells, areas of perivascular cell growth and collections of colloid, but metas-

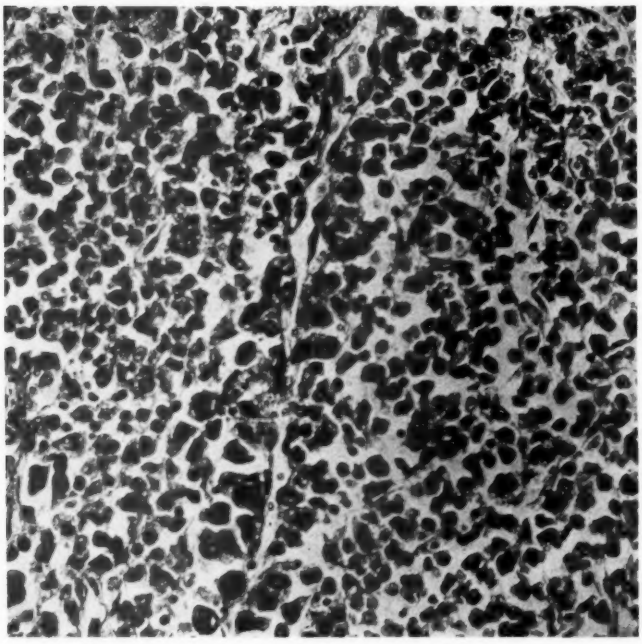

Fig. 1. Case 1. Diffuse malignant thymoma. Polyhedral cells attached to capillary wall and growing diffusely. Scanty lymphocytes.

tases were limited to the pleura. The tumor described by Hahn and Thomas reached demensions of 26 x 18 x 19 cm. in one year.

Constitutional symptoms suggesting a sympathetic disturbance of the chromaffine system are not observed, but Gabcke records for his case that the adrenals were very large and the skin pigmented. In a notable group of cases thymic tumor has been associated with myasthenia gravis (Oppenheim, Weigert and Laquer, Buzzard). Of 45 cases of myasthenia gravis Mandelbaum and Cellar found thymus lesions recorded in eleven. The thymic tumor has usually shown the structure of "lymphosarcoma" mingled with epitheloid cells. In Hun's case the epithelioid cells were abundant but showed no tendency to form Hassall's corpuscles, while plasma cells, eosinophile cells and focal hæmorrhages are often present. Mandelbaum and Celler found a tumor composed of small concentric groups of polyhedral cells, while the numerous vessels were sheathed with lymphocytes and surrounded by tumor cells. The tumors are usually of moderate size, and in several cases the lesion was regarded as simple hyperplasia (Link, Burr, Buzzard).

Throughout the skeletal muscles and often in the organs are found foci of lymphocytes with varying numbers of polynuclear leucocytes, and eosinophile, plasma, or epithelioid cells. Weigert and Laquer regarded these lesions as metastatic foci, while others consider them as of local inflammatory origin. Their occurrence favors the view that some thymic tumors are manifestations of an infectious granuloma.

REPORT OF THREE CASES OF THYMOMA

CASE 1 (6470). *Thymoma with extensions throughout neck, mediastinum, and axillæ. Acute febrile course, duration seven months. Suppuration and necrosis. Death from asphyxia. No distant metastases. Tumor composed of round, cubical, and cylindrical reticulum cells.*

Clinical abstract: A. C., female, 19 years. Family history negative. Had scarlatina in childhood. One year ago noticed slight œdema of feet. Illness

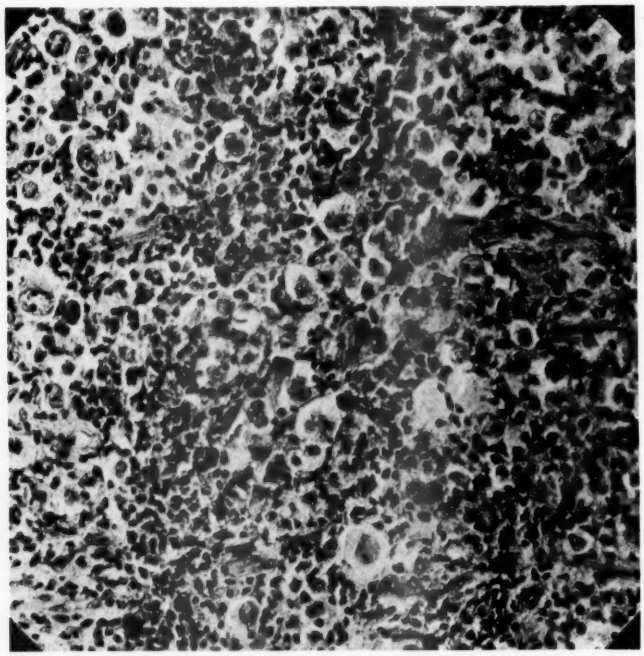

Fig. 2. Case 2. From presternal mass. Abundant giant cells, many polyhedral reticulum cells, scanty lymphocytes.

began in August 1914 with a swelling of left side of neck, which, after reaching the size of an egg, largely regressed. The swelling was referred to two decayed molar teeth which were extracted and found to be the seat of root abscesses. The swelling soon recurred and the whole right side of neck from ear to shoulder became much swollen. There was irregular fever and loss of weight. October 15, left side of neck became involved and in December the right axilla was swollen. December 30, an abscess in the right side of neck was opened and some tumor tissue removed.

On admission to the General Memorial Hospital January 25, 1915, the patient presented very extensive swelling of both sides of the neck from ears to shoulders and involving both axillæ, especially the right, where the tumors were bulky, diffuse, and ulcerating. There was œdema of the face and slight exophthalmos of right eye. The neck was immovable and pressure on the trachea and larynx caused constant dyspnœa. The temperature ran from 99 to 103°F. Percussion revealed a tumor mass behind sternum and much restriction of respiration. The other organs and lymph-nodes were negative. Exitus February 9.

Autopsy: February 10, 1915. Body moderately emaciated and anæmic. A bulky, diffuse tumor mass extends from ears over both sides of neck, over right shoulder, and into right axilla. Ulcerating areas present in neck and over the shoulder. The right humerus is displaced by bulky tumor masses in axilla and considerable masses appear in left axilla. The right breast is swollen and invaded by tumor-tissue. On dissection the tumor is found to extend from the base of the skull tightly incasing the pharynx, larynx, trachea, and vessels, to the upper border of the pericardium and root of lung. In the region of the thymus it is very dense and fused with all adjoining structures and with the sternum. The larynx is tightly compressed by firm masses of tumor which surround thyroid cartilage, sinuses, tonsillar regions, and base of tongue. Many tumor nodules protrude beneath the masses but the surface epithelium is everywhere intact. The lung is not involved but the pleura is invaded from the axilla, through the third intercostal space. The right lobe of the thyroid is diffusely invaded. The tumor-tissue is firm, elastic, lobulated, of peculiar lemon yellow color, and except in suppurating areas, free from necrosis. The bronchial lymph-nodes are invaded but there are no extensions below this point and no metastases.

Lungs, congested, œdematous; liver shows slight cloudy swelling; spleen slightly enlarged, soft, follicles invisible; kidneys show slight irregularities in cortical markings; adrenals normal; gastro-

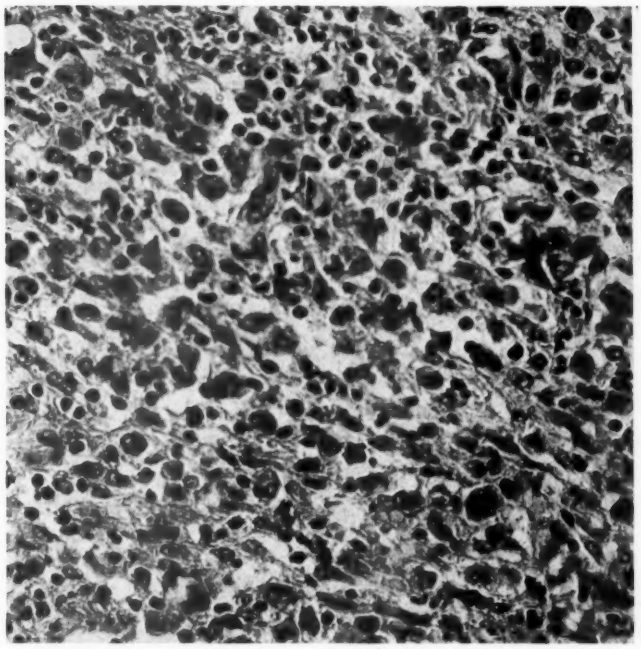

Fig. 3. Case 3. Coherent network of large fusiform and polyhedral reticulum cells fibrosing at edge. Scanty lymphocytes.

intestinal tract and genital organs normal; no traces of suppuration were found in upper or lower maxillæ.

Microscopical structure: The tumor has the general structure of a large cell lymphosarcoma but is much more vascular and presents much more fibrous tissue than a lymphosarcoma. On closer study the prevailing cell is found to be a medium sized polyhedral or cubical cell of epithelial character. The nuclei are large and vesicular, the nucleoli prominent, and the cytoplasm opaque and acidophile. The arrangement is not diffuse, but the cells are applied to the walls of numerous capillaries in cubical or cylindrical form and often in palisade fashion or yielding a pseudopapillary structure (Fig. 1.) Mitoses are very numerous. Scattered lymphocytes appear throughout the section. Giant cells appear in two forms: One resembles the myeloid giant cells with bulky multilobed nuclei. The other is a large pale vacuolated cell with shrunken nucleus, and containing englobed detritus. It may be traced to the chief cells. The whole tumor is subdivided into many small lobules by rather dense fibrous tissue, and the thickening of many capillary walls adds to the density.

Epicritical. The chief features of interest in this case are: the acute febrile course and the early simulation of an infectious process following alveolar abscess; the very rapid extensions during the later course; the absence of metastases; and the characteristic structure. The diagnosis of a thymic origin is based on the gross anatomy which showed the densest portion of the growth in the region of the thymus, on the mode of extension peculiar to thymic tumors, and on the structure. The tumor proved to be not a lymphosarcoma but a peculiar growth of epithelioid cells and giant cells as observed in other thymic tumors. The absence of Hassall corpuscles may be referred to the rapid growth of the tumor which was distinctly neoplastic and malignant.

CASE 2 (6406). *Perforating sternal tumor originating in the thymus. Enlargement of nodes in both axillæ and behind clavicle. Duration 2 years, active course four months. Regression under X-ray treatment. Structure of tumor, giant cell thymoma.*

Clinical notes. Mr. J. N., age 32, plasterer. A brother died of pulmonary tuberculosis. Typhoid fever at 8 years. Had severe colitis shortly before beginning of present illness. Has had several

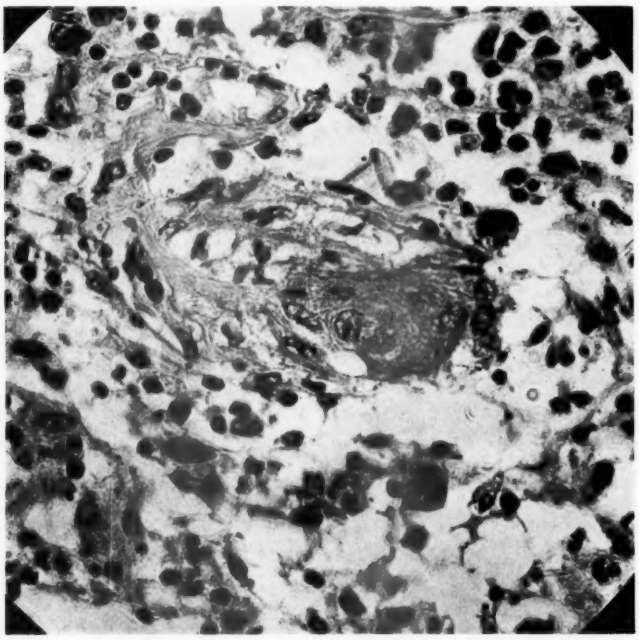

Fig. 4. Case 3. Hassall corpuscle forming in reticulum. Polyhedral tumor-cells attached to reticulum. Scanty lymphocytes.

attacks of tonsillitis. About January, 1913, noticed beginning tenderness of upper part of sternum and enlargement of lymph-nodes in both axillæ. These symptoms increased slowly but he continued at work. In July, 1914, he began to suffer from fever at night, and the axillary nodes increased in size. There was now a feeling of fullness in the chest and a tendency to cough while talking. In November, 1914, he became severely ill and was confined to bed with fever at times as high as 106°F. The sternum became more tender and a swelling appeared at the second and third interspaces. In December this swelling was incised and a portion of tissue removed for examination. On admission to the General Memorial Hospital, January 7, 1915, the patient was somewhat emaciated, temperature running between 99 and 103°C. There was a fungating ulcerated tumor, 5 x 8 cm. over upper portion of sternum. A soft elongated tumor mass appeared from behind the right clavicle. The nodes in both axillæ were enlarged, those on the right side as large as a walnut. The cervical nodes were not affected but the inguinal nodes were slightly enlarged. The spleen was barely palpable. Percussion indicated the presence of a mass in the upper mediastinum, and the X-ray revealed a distinct shadow extending 14 cm. downward from the sternal notch and 13 cm. laterally.

Under heavy X-ray treatment the ulcerating tumor healed and the enlarged nodes disappeared, the X-ray shadow contracted, the patient greatly improved in strength and nutrition, the temperature became normal, and he was discharged, to return regularly for observation.

The tissue removed from the sternal tumor presented a structure resembling Hodgkin's granuloma with excess of peculiar giant cells. The giant cells are large rounded or polyhedral with light staining cytoplasm, nuclei multilobed and hyperchromatic or multiple and vesicular, and with very prominent strongly acidophile nucleoli. They are larger than the giant cells of Hodgkin's granuloma and somewhat resemble the myeloplaques of bone marrow. They are numerous and appear uniformly over the entire section. The derivation of the giant cells seems traceable to more numerous smaller rounded or polyhedral epithelioid cells which made up the bulk of the tissue. In some areas the smaller cells are exclusively present while other portions consist chiefly of giant cells. Both frequently show mitoses. The stroma is composed of small arterioles and capillaries with cellular walls along which the main tumor-cells are often arranged as cubical or columnar epithelium. Throughout the section lymphocytes appear in moderate numbers. Necro-

sis appears in a few small areas, and also affects isolated giant cells (Fig. 2).

Interpretation. The existence of a large mediastinal tumor is clearly indicated by auscultatory and X-ray signs. The early perforation of the chest wall is a notable feature which has previously been observed by Le Tulle, Zniniewicz, and Seebohm. The diagnosis of a thymic tumor is based not only on the physical signs but especially on the histological structure. The finer structural details differ widely from those of ordinary lymphocytoma or reticulum-cell sarcoma, and accord closely with those of other cases of this series. The whole process presents the characters of a peculiar infectious granuloma rather than of a true neoplasm, and in many respects resembles Hodgkin's granuloma. The prompt regression under X-ray treatment also suggests a granulomatous nature. Although the inguinal nodes were slightly enlarged there was no definite systemic involvement.

CASE 3. (3742). *Slowly progressive thymoma of granulomatous type, suggesting Hodgkin's disease, in a subject of 50 years. Duration 2 years. Large very dense circumscribed mediastinal tumor. No metastases. Structure of cubical and polyhedral reticulum cells, with Hassall's corpuscles and many peculiar giant cells.*

This case has already been reported by Symmers as a possible example of transformation of Hodgkin's granuloma into sarcoma. The possibility of a thymic origin was considered by Symmers and the later study of the case in the light of other cases and especially the demonstration of Hassall's corpuscles lead me to conclude that the tumor is a thymoma.

Clinical abstract. Patient, female, 56 years, began to suffer pain in right shoulder in November, 1908, which soon extended to left shoulder. Attacks of febrile jaundice and œdema of legs were noted in March, 1909. In November, 1909, a variable swelling appeared above right clavicle. In May there was dyspnœa and dry cough. July 1, a small tender mass appeared in left side of neck, soon followed by enlargement of right side of neck and right breast, dilatation of chest veins, and severe dyspnœa. The chest was twice aspirated of clear fluid. The supraclavicular and suprasternal nodes were enlarged but the axillæ remained free. With increasing dyspnœa and general œdema of right arm, chest and legs, the patient succumbed, October 29, 1910. Duration, total, 24 months; after appearance of cervical tumor, 12 months.

Autopsy revealed a firm lobulated lemon yellow tumor, 18 x 11 x 15 cm. in the upper mediastinum, overlapping the pericardium, pushing heart downward, and incasing the trachea and great vessels. Above, it invaded the lower pole of the thyroid. The trachea was slightly displaced to the left and its wall invaded for a length of 8 cm. by nodules which extended to the submucosa and caused erosion of lining epithelium. The mass extended from sternum to spine but did not invade lung. No metastases were demonstrated. The general lymphatic system, spleen and bone marrow were unaffected and the other organs were negative.

The tumor was remarkably firm, solid, resistant, and sharply defined, and on section exhibited many small lobules of rather uniform size surrounded by dense connective tissue.

Microscopical structure. The tumor presented the general appearance of Hodgkin's granuloma with excess of peculiar giant cells and unusual fibrosis. The chief cells were large with hyperchromatic nuclei, suggesting a transformation into sarcoma.

On analysis from the standpoint of thymoma characteristic features are revealed (Fig. 3). The chief cells are not large lymphocytes, but cubical, cylindrical, polyhedral, elongated, and very irregular cells with vesicular nuclei and prominent nucleoli. Most of these form parts of a reticulum sometimes inclosing capillaries to which many of the cells are attached. In the meshes of the reticulum lie loose tumor-cells, and a uniform admixture of lymphocytes. The reticulum cells make the chief feature of the tumor and in places these pale cells form concentric groups resembling Hassall's corpuscles (Fig. 4). Giant cells are very numerous and of all sizes. They present large multilobed nuclei almost filling the cell body. They may be traced to the proliferating cells of the reticulum. Mitoses are very scanty. The tumor lobules are small or large and are surrounded by dense or cellular fibrous tissue which penetrates the lobules, is continuous with the reticulum, and gives the impression of a progressive sclerosis in a once more cellular tumor.

The diagnosis of thymoma is based on the form, location, density, circumscription, and color of the tumor in the gross and on its microscopical structure. This structure differs notably from lymphosarcoma or Hodgkin's granuloma. As noted by Symmers its neoplastic characters are not pronounced. The chief cells are not round, or lymphocytic nor do they resemble lymphatic reticulum cells, but are cubical or elongated or even cylindrical. The reproduction of Hassall corpuscles, while imperfect, is quite as complete as in many such bodies in the normal thymus. The tumor arises from the reticulum cells of the thymus while many lymphocytes persist in the process and contribute to the bulk of the tumor. The giant cells are also different from those of Hodgkin's granuloma. They are often very large, the cytoplasm is opaque and acidophile and nuclei are very hyperchromatic. The history and the indefinite neoplastic properties suggest that the process, like Hodgkin's disease, was of infectious and inflammatory origin.

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THE PHYSIOLOGICAL METHOD OF TENDON TRANSPLANTATION

III. EXPERIMENTAL AND CLINICAL EXPERIENCES[1]

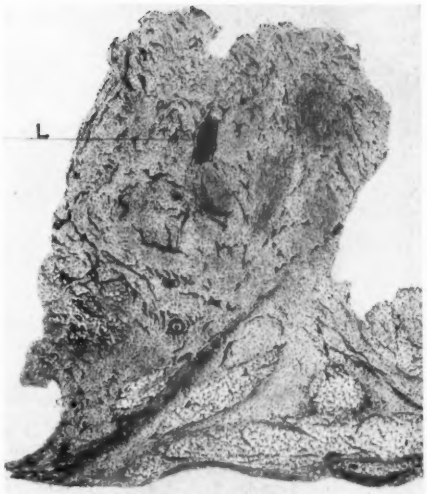
BY LEO MAYER, A.M., M.D., NEW YORK

EXPERIMENTAL EXPERIENCES

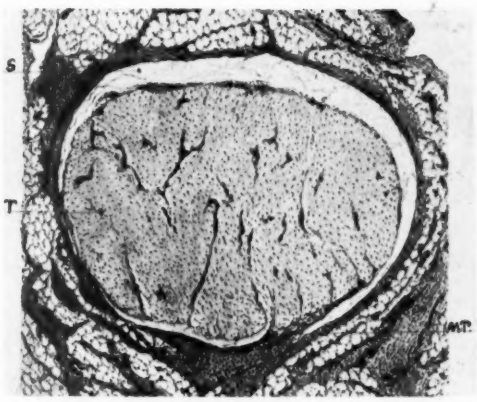
THE experimental basis of the physiological tendon transplantation was worked out in 1912 by the experiments conducted by Dr. Henze and myself in the clinic of Professor Lange of Munich. These experiments showed conclusively that post-operative adhesions could be prevented by restoring the normal relationship between the tendon and the sheath.

I undertook further experimental work to test the efficiency of the fixation method outlined in the previous paper and thus to determine when it was safe to allow the transplanted tendon to function. I also wished to trace the course of events in the tendon, in the transplanted muscle, in the sheath, and in the surrounding tissues subsequent to the operation. The material for this study was derived from eight operations on dogs and five secondary operations performed by Professor Biesalski on patients of his clinic. These secondary operations were performed 10, 16, 24, and 48 days after the original operations, and in the fifth case, after 3 years. It was possible without injury to the patient, not only to examine the tissues macroscopically, but to remove small sections for microscopical study. In this way extremely valuable data were secured.

[1] For first article in this series, see February, 1916, p. 182; for second article, see March 1916, p. 298.



1. Cross section of the traumatized, transplanted tendon of the tibialis anticus 24 days after operation. The endotenon has proliferated to a marked degree; the surface of the tendon is irregular, the mesotenon is thickened and scarred. Here and there are minute hæmorrhage in the tendon. *L*, hymphocytes and giant cells surrounding a localized hæmorrhage.

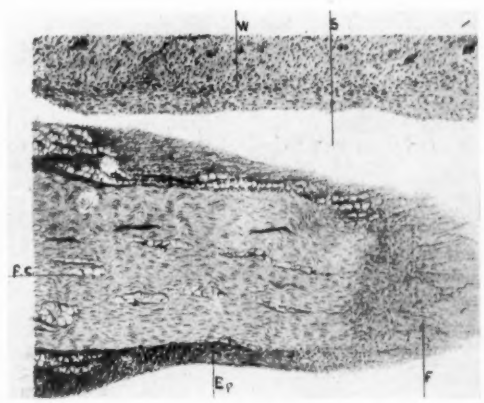


2. Cross section through the transplanted tendon of the peroneus longus in its course through the sheath of the tibialis anticus, 17 days after operation. Leitz. obj. 1. Oc. 4. T. 160. In the cavity of the sheath are delicate connective tissue strands — the result of the slight trauma incidental to the operation. They are sufficiently elastic not to impede the free gliding of the tendon. Uniting the tendon to the floor of the sheath is a new formed mesotenon. The tendon itself is microscopically normal, except for a slight proliferation of the endotenon and hypertrophy of the blood-vessels. *S*, cavity of sheath; *T*, endotenon slightly hypertrophied; *Mt*, new formed mesotenon.

1. THE FIXATION OF THE TENDON

It will be remembered that the physiological method of fixing the tendon consists in implanting it into the bone or cartilage, preferably at the site of the paralyzed tendon, so that it can be sutured to tendon as well as to the bone. The fixation has to meet the double demand of mechanical and of physiological security. By the latter I mean the union which occurs between the tendon and the surrounding tissues during the normal healing process. To insure this firm physiological fixation, the living tendon-cells, proximal to the fixation suture, should lie in direct contact with the traumatized periosteum.

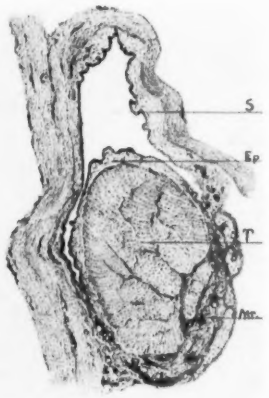
The experiments had to solve two questions: First, how long does the mechanical fixation of the suture last? Second, when does the physiological fixation begin? It is evident that if the mechanical fixation lasts until the tendon has actually healed fast to the new point of insertion, active exercise and electrical stimulation of the transplanted muscle can be begun immediately after the operation without danger of tearing away the tendon



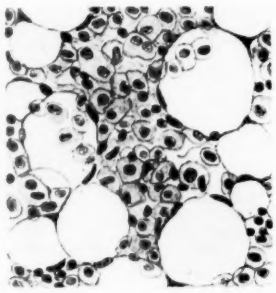
3. Cross section through the transplanted tendon of the flexor longus digitorum in its course through the sheath of the tibialis posticus, 17 days after operation. Leitz. obj. 1. Oc. 4. T. 140. Weigert's elastica stain.

The tendon lies free within the cavity of the sheath, and has the normal range of motion. Degenerative changes have, however, occurred: proliferation of the epitenon, the development of elastic fibers in the epitenon and of fat-cells between the tendon bundles. *W*, Wall of sheath; *S*, cavity of sheath; *F*, elastic fibers in the epitenon; *Ep*, epitenon of tendon; *F. C.*, islands of fat-cells.

4. The gastrocnemii of a dog. To the left, the muscle after 2 months post-operative immobilization under maximum tension. To the right, as contrast, the normal gastrocnemius of the same dog. The overstretched, immobilized muscle weighs one-half the normal and shows marked fatty degeneration. *N*, normal gastrocnemius, *P*, pathological gastrocnemius.

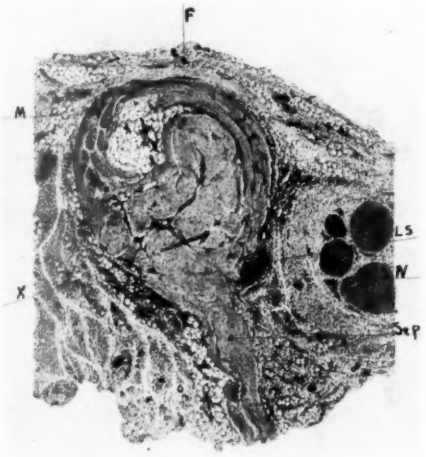


5. Cross section through the transplanted tendon of the extensor proprius hallucis in its course through the sheath of the tibialis anticus, three years after the operation. Leitz. obj. 1. Oc. 1. T. 150. The tendon, sheath, and mesotenon are normal. The epitenon is somewhat hypertrophied. Clinically and at the secondary operation the tendon showed the normal range of motion. *S*, cavity of the sheath; *Ep.* epitenon; *T*, tendon; *Mt*, mesotenon.



6. Fat transplanted with the tendon of the peroneus longus, 17 days after the operation. Leitz. obj. 5. Oc. 1. T. 160. Between the fat-cells have appeared large pale-staining, mononuclear and multinuclear cells. Marchand and Maximow have observed similar cells after experimental transplantation of fat.

from its moorings. My observations show clearly that, when the tendon is properly anchored, this overlapping of the mechanical and physiological fixation actually occurs,



7. Cross section through the fascial-plastic. Seventeen days after operation. Leitz. obj. 1. Oc. 1. T. 140.

The fascia of the anterior muscular compartment has been inverted so that its deep surface, covered with loose gliding tissue, lies superficial and serves as a bridge for the passage of the peroneal tendon from the lateral to the anterior muscular compartment. The gliding tissue is microscopically, as well as macroscopically, normal. *F*, fatty gliding tissue; *LS*, Lembert suture; *N*, the musculocutaneous nerve; *Sep*, septum intermusculare anterius; *M*, inverted fascial flap of the anterior muscular compartment; *X*, fascia of the peroneal compartment (doubled on itself).

and that therefore the early functioning of the tendon is a safe procedure.

a. *Dog experiment. Tendon of the extensor longus digitorum drawn through the sheath of the tibialis anticus and fastened to its point of insertion.* Examination after 4 days: fixation suture fast in tendon; traction on muscle produced flexion of foot without tearing away the tendon from its new insertion. As soon, however, as the suture was divided the tendon tore away; that is, the physiological union between tendon and bone had not yet occurred.

b. *Katie K. Transplantation of flexor longus hallucis through sheath of the peroneus brevis for complete paralysis of the pronator muscles.* After 1 week action exercises were begun. The tendon, however, did not function satisfactorily. Therefore 10 days after the original operation the operative site was exposed: though the tendon was freely movable within the peroneal sheath it was adherent at the point where it passed through the septum intermusculare posterius. After the adhesions had been divided, electrical stimulation of the flexor longus hallucis produced abduction and eversion of the foot, thus showing the security of the tendon fixation. A silver electrode was placed against the muscle-belly, sutured into position and its free end brought out through the bandage. Thereafter, daily electrical stimulation. Two weeks later, the patient could actively pronate the foot.

c. *Herbert B. Peroneus longus for tibialis anticus.* Secondary operation 16 days later. The tendon freely movable within the sheath of the tibialis anticus, but so firmly adherent to the internal cuneiform as to resist a traction of 8 pounds.

d. *Erna Z. Transplantation of flexor longus digitorum to the scaphoid.* At time of operation a silver electrode was sutured against the muscle-belly. Daily electrical stimulation was begun the day subsequent to the operation. Examination at secondary operation, 48 days later, showed the tendon to be firmly united to the scaphoid. When the muscle was faradized it could supinate the foot against considerable manual resistance.

e. *Hermann G. Extensor longus hallucis for tibialis anticus.* Secondary operation three years later. The insertion of the transplanted tendon could not be distinguished macroscopically from that of a normal tendon; even microscopically, were it not for the cellular reaction surrounding the silk sutures, it would have been impossible to recognize that the tendon had been transplanted.

The physiological method of tendon fixation thus enables the surgeon to begin postoperative exercises immediately after the operation, since it assures mechanical as well as physiological stability.

When other methods of fixation are used the early mobilization tends to tear the suture out of the tendon. For example, a rabbit experiment performed with Dr. Henze: The divided extensor longus digitorum was sutured by the Lange stitch leaving a gap of one centimeter between its ends. On the third day electrical stimulation of the muscle was begun. At first the toes of the rabbit responded to the stimulation; but by the eighth day they no longer moved, though the muscle itself could be felt to contract. Autopsy on the twentieth day showed that the suture had torn out of the distal tendon stump.

The method of fixation I have adopted is by no means the only physiological means of implanting the tendon. Drawing it through a hole drilled in the bone (Mueller, Putti, Whitman) or fastening it to the bone by means of a nail (Codivilla, Jones) also meet the demands of the physiological method. However, the first is somewhat more complicated, the second necessitates introducing a non-absorbable foreign body and consequently carries with it the danger of subsequent infection.

2. CHANGES IN THE TENDON SUBSEQUENT TO THE TRANSPLANTATION

The tendon itself is peculiarly susceptible to traumatism. It must be handled with as much delicacy as a nerve. In one of the earlier operations where the truth of this fact was not appreciated and the tendon was grasped with forceps, the result was a marked hypertrophy of the endotenon. The entire structure of the tendon changed (Fig. 1), so that it looked more like scar-tissue than like tendon. In the later cases, the transplanted tendon showed a slight hypertrophy of the endotenon and of the blood-vessels (Fig. 2) and was slightly softer than the normal; otherwise no changes were noted.

Immobilization of the tendon tends to its degeneration. This important fact, already demonstrated by the transplantation experiments of Lewis and Davis was emphasized by the results of a secondary operation 24 days subsequent to transplanting the flexor longus digitorum through the sheath of the tibialis posticus. For 24 days the tendon had been immobilized. Though it was still freely movable within the sheath of the tibialis

posticus, it was much softer than normal, and microscopically showed two significant changes (Fig. 3): first, the appearance of fat-cells between the tendon bundles; second, the development of elastic fibers in the epitenon (the thin connective-tissue coating of the tendon within the sheath).

It is probable that these regressive changes disappear when the tendon begins to function, for a specimen examined after 3 years of active function, was microscopically normal, despite a 5 weeks' preliminary immobilization.

3. CHANGES IN THE MUSCLE SUBSEQUENT TO OPERATION

The muscle also degenerates subsequent to the operation if it is not allowed to function. Particularly marked are the changes when the tendon has been sutured under abnormally high tension. In the article dealing with the physiology of tendons I emphasized the fact that normally a resting muscle during narcosis exercises no traction on the tendon; that is, the tendon is not under tension. Robert Jones, and before him, Hugh Owen Thomas, have in turn for many years taught us that an overstretched muscle degenerates to such a degree as to seem paralyzed. This significant physiological truth must be applied to the technique of tendon transplantation. The surgeon must be as careful not to overstretch the muscle by suturing the tendon under abnormal tension as he must be not to overstretch the extensor muscles of the wrist in a case of lead paralysis. Just as he conserves the normal muscular tone of the extensors by splinting the hand in a position of extension, so he conserves the transplanted muscles by suturing the tendon under normal tension.

Figure 4 shows graphically the effects of overstretching the muscle combined with immobilization. The muscles pictured are the gastrocnemii of a dog;—on the right, the normal unoperated on the left the operated. The Achilles tendon 2 months previously had been divided, reunited under the greatest tension possible, and the leg fixed in plaster bandage. At autopsy the overstretched muscle weighed one-half that of the normal, had shrunk to one-half the normal size and showed microscopically and macroscopically, extensive fatty degeneration. This result was substantiated by five similar operations and by control experiments in which simple immobilization under normal tension caused only slight degeneration.

4. THE SHEATH SUBSEQUENT TO OPERATION

When the tendon has been drawn through the sheath of the paralyzed tendon, the complete return to the normal does not occur throughout its entire length. Owing to the unavoidable slight post-operative oozing, delicate connective-tissue strands form between the tendon and the sheath (see Fig. 2). These strands are so delicate and elastic as to offer no serious hindrance to the gliding of the tendon. In some portions of the sheath even these delicate bands are absent and almost the normal histological picture is seen (Fig. 5).

5. THE SURROUNDING TISSUES

The loose fatty tissue investing the tendon, (the paratenon) shows only slight changes when transplanted with the tendon. Here and there the fat-cells are replaced by peculiar cells twice the size of the white blood-corpuscle, frequently containing two or more nuclei (Fig. 6). These cells have also been observed by Maximow, Marchand, and by Rehn in fat transplantations. It is well, however, not to transplant much fatty tissue with the tendon, for in case a hæmorrhage occurs into the fat, it is replaced by fibrous connective tissue and impedes the gliding of the tendon.

Where the tendon sheath has been opened to allow the transplanted tendon to enter, delicate adhesions also form, which close the opening, but do not seriously interfere with the motion of the tendon, provided it is allowed to function early.

If, however, the tendon is drawn through the interosseous ligament or through a fascial septum or if the periosteum is injured dense adhesions occur which render function of the tendon impossible. This important fact has been proved by numerous observations. In several rabbit experiments performed with Dr. Henze where the periosteum had been

traumatized, the tendon was invariably found adherent. In a secondary operation on a patient of Professor Biesalski, where one year previous the flexor longus hallucis had been drawn through the interosseus membrane and sutured to the extensor longus hallucis — needless to say this operation was performed before the physiological method of transplanting had been introduced — the muscle was found tightly bound to the interosseus membrane. In the case already referred to (Katie K. — transplantation of the flexor longus hallucis through the sheath of the peroneus brevis), secondary operation 10 days later showed the tendon adherent exactly at that point where it was in contact with the traumatized fascial septum intermusculare posterius through which it has been drawn en route to the peroneal sheath. Within the sheath no adhesions were present.

It was because of these and similar observations that I devised the *fascial plastic* I described in the previous paper.

The plastic, it will be remembered, consists in inverting the fascia, so that its deep surface, covered with loose, gliding tissue (paratenion), should serve as a bridge for the passage of the peroneal tendon from its original fascial compartment to that of the tibialis anticus. Here also I was able to obtain positive proof of the effectiveness of the plastic at a secondary operation 16 days subsequent to the transfer of the peroneal tendon for the paralyzed tibialis anticus. Not only macroscopically, but microscopically (Fig. 7) the fascia and the paratenon were normal. No adhesions were present between tendon and the inverted fascia, the paratenon had conserved its normal glistening appearance, and the tendon glided as freely over the fascial bridge as within the sheath of the tibialis anticus.

The physiological method of tendon transplantation is thus given experimental sanction not only by animal experiments but by unusually convincing observations during secondary operations on human beings.

Clinical Experiences

Equally convincing of the rationality of the method are the clinical results. During the last 4 years Professor Biesalski and I have performed some 50 tendon transplantations. In only one instance have I noted post-operative adhesions which interfered with the function of the tendon (the operation already referred to in which the flexor longus hallucis was transplanted for the peroneus brevis). Here the adhesions occurred exactly at the point where we had violated a physiological principle. In all other instances the transplanted tendon has behaved like a normal and has helped to restore the normal muscle balance. To achieve these results we have tried to be physiological not only in the operative technique but in the treatment before and after operation.

In the pre-operative treatment and in the selection of cases three principles are of paramount importance: First, never operate, no matter how long the interval since the incidence of the paralysis until the paralyzed muscles have been given adequate postural treatment. Frequently the paralysis is merely apparent, and the overstretched muscles recover their tone rapidly when their fibers are given a chance to contract. This lesson in muscle dynamics, which was preached 40 years ago by Thomas, frequently reiterated by Robert Jones, and substantiated experimentally within the last few years by Stoffel and by me, is to be adhered to in all instances except one; if the triceps zuræ (gastrocnemius and soleus) is paralyzed, do not wait long before operating, since delay almost always means the development of a talipes cavocalcaneus.

Second, never attempt the impossible. The disrepute into which tendon transplantation has fallen, notably in the Parisian and Vienna schools, is due entirely to its abuse. The tendon transplantation should never be used to correct a bony deformity. On the contrary, bony deformities must be corrected preparatory to the tendon operation. The sole purpose of the transplantation is the restoration of the normal muscle balance. When too many muscles are paralyzed this is impossible. The dictum of a noted German orthopedist that three muscles suffice for the motions of the foot, cannot in my opinion bear the test of experience. It is far better

to arthrodize the foot, or perform Whitman's astragelectomy, or even to replace the paralyzed muscles with appropriate splints, than to attempt tendon plastics with insufficient material. I have never performed a tendon transplantation on the foot when more than three muscles were paralyzed, and only then with the full realization that the operation could merely improve the function of the foot, not restore it to the normal. Most suited to the operation are cases where one or two muscles are absent, or in spastic cases where a group of muscles — the peronei or the supinators, for instance — are overactive. There the transplantation, if properly executed, gives gratifying results.

Third, never operate when muscles are present capable of assuming the function of the paralyzed. This is particularly true of the quadriceps paralysis. Here, if a strong gluteus maximus and a strong triceps suræ (gastrocnemius and soleus) are present the action of the quadriceps can be dispensed with.[1] Walking, standing with bent knees, climbing stairs, rising from a low chair are all made possible by the vicarious function of the gluteus and gastrocnemius. Under such conditions to risk an operation, no matter how tempting, would justly draw down the anger of the gods.

In the *actual execution* of the operation the *physiological technique* must be adhered to scrupulously. The operations are technically difficult. No one should attempt them without ample practice on the cadaver. A peculiarly accurate anatomical knowledge is necessary: the operator must know to a nicety the exact location of the tendon sheath, the level of the fascial planes, the line of insertion of the mesotenon, and a score of other details not given in the anatomical textbooks. Only then can he hope to operate with a minimal degree of trauma and with the maximum efficiency.

Three rules are again all important in the post-operative treatment.

1. Never undertake the operation unless the after-treatment can be effectively and conscientiously carried out under your direction. To consider the operation as the final link in the treatment would be as foolish as concluding a gastro-enterostomy before the mucosa suture had been completed.

2. Remember that no matter how skilful the surgeon, no matter how accurate the physiological technique, adhesions and degeneration of the tendon are apt to occur unless early function is instituted. Whenever the typical physiological fixation has been possible, it is safe and wise to begin active exercise of the transplanted tendon a few days after the operation. In young children to facilitate the early function I implant a silver electrode at the time of the operation, and can thus stimulate muscular contraction with far less pain than through the resistant skin. Of course, there are exceptions to the rule of early function. It is sometimes impossible to perform the ideal physiological fixation; for instance, in transplanting the flexor carpi ulnaris for the paralyzed extensor the tendons must be sutured to one another — a far less certain procedure than implanting the tendon into bone. Then 2 or 3 weeks must elapse before motion is allowed. Or again, in the transplantation of the flexor longus hallucis and the peroneus longus for the triceps suræ an immobilization of 3 or 4 weeks is usually necessary to allow the proper shrinkage of the posterior capsule of the ankle-joint. The immobilization is without danger since adhesions are almost excluded by the nature of the operation.

3. Remember that the transplanted tendon is not quite as strong as the normal, and that usually it is called upon to do more than the normal amount of work. Therefore, it should be protected by suitable apparatus and strengthened by carefully graded exercises. This phase of the after-treatment must be continued until the transplanted muscle can actually do the work required of it.

Conclusions

In these three papers I have tried to outline a system of tendon operations based upon the anatomy and physiology of the structures involved. In the first paper I explained first the inception of the work as the natural outgrowth of an experimental study of tendon plastics, in which the fundamental principle

[1] See American Journal of Surgery, December, 1914.

of the physiological method — the restoration of the normal relationship between tendon and sheath as formulated by Biesalski in 1910 — was verified experimentally; second, I described the complicated finer anatomy of the tendon and the related connective-tissue structures — the sheath, mesotenon, paratenon, epitenon and endotenon; and third the hitherto unknown basic facts of tendon physiology—the mechanism of tendon motion, and the laws of tendon traction and tension.

In the second paper I formulated the operative technique of the physiological method and described three of the 20 operations which my experience has led me to consider physiological. This particular number of operations is not to be regarded as final. It is to be hoped that helpful competition and co-operation will soon enable us to include other operations in this category.

In the third paper I told how the physiological method has been substantiated by animal experiments, by the results of secondary operations and by four years of clinical experience.

I wish again to emphasize my deep indebtedness to my friend and former chief, Professor Biesalski. The entire structure of the physiological method rests upon his utilization of the sheath as the physiological preventive of adhesions. To him I am indebted, not only for unusual experimental and clinical opportunities, but for the constant encouragement of his stimulating personality.

To Dr. Henze of New Haven also I feel particularly grateful, since he was the first to interest me in the many problems of tendon operation. During our work together in Munich in 1912 the germs of the physiological method were sown. To Dr. Walter M. Brickner of New York I am indebted for many helpful suggestions, and to Mr. Robert Jones of Liverpool for words of encouragement and for invaluable lessons in the laws of tendon surgery.

No one realizes more fully than I the shortcomings of these papers. For the physiological method, however, I offer no apology. It is a safe, conservative procedure which in the hands of the competent surgeon is certain to help many of our patients. I must again warn the unwary not to attempt the operations. They are technically difficult. They should not be performed unless the surgeon can conscientiously satisfy the following qualifications: First, he must be the absolute master of tendon anatomy — and I refer not to their gross topography as given in the standard textbooks but to their finer structures and relations; second, he must have performed the operations on the cadaver sufficiently often to know their every detail; third, he must have sufficient general surgical skill to operate with speed, accuracy, and minimal traumatism. Only when all these qualifications are satisfied is it fair to pronounce judgment upon the merits of the physiological method of tendon transplantation.

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DEPARTMENT OF TECHNIQUE

RECTAL DRAINAGE OF APPENDICEAL PELVIC ABSCESS

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THE literature of appendicitis has been exhausted from all its angles. However, the definite indication of this type of drainage in selected cases, as well as the scarcity of the literature on this particular subject, justifies its consideration.

An acute appendiceal process may be associated with, or followed by, an abscess, the location of which may vary in its anatomical position. The usual appendiceal abscess is situated in the vicinity of the appendix, either on the parietal peritoneum or between loops of bowel, the level and location of which depend upon the position of the appendix, which has a wide range of excursion. In a less common group of cases, the abscess may spread backward and upward, the lumbo or posteroparietal type, or upward and forward, the anteroparietal type, or downward, the rectal or the pelvic type.

A. Frankel, Penzoltd, Riedel, Curshman, have called attention to the necessity of rectal examination in acute appendiceal processes early in the history of appendicitis. The etiology of the pelvic type of appendiceal abscess is ordinarily the appendiceal pus which gravitates into the pelvis, particularly when the appendix hangs over the brim of the pelvis; in other words, it is a gravity abscess. This process is naturally favored by lack of omental or intestinal adhesions, which ordinarily tend to limit the abscess in the appendiceal zone. In the opinion of Archibald MacLaren of St. Paul, practically all pelvic abscesses in the male are appendiceal in origin. The cases in which there are two appendiceal abscesses, either distinctly separate or communicating with one another, demand another explanation. A. C. Bernays collected the serous fluid from the pelvic floor of a number of cases of acute appendicitis with beginning peritoneal reaction, but without pus at the time of operation, and found that it contained a rich bacterial flora, which incubated on suitable media developed very prolifically. Sonnenberg also called attention to the reaction serous peritonitis which accompanies an acute intra-abdominal focus. This fluid gravitates and may subsequently become infected. If this theory were true, it would be logical to assume that the Fowler position, so extensively employed in this country in acute appendicitis, may favor, in a number of cases, the late development of pelvic abscesses secondary to an acute appendicitis.

Bérard and Patel divide the pelvic abscesses into two classes: (a) peri-appendiceal, in which there is direct connection with the abscess surrounding the appendix; and (b) para-appendiceal, in which the abscess is above the pelvic brim and has no direct connection with the abscess below. Broca (1) also distinguishes two types of appendiceal abscesses: the superior and inferior pelvic. The first originates near the superior straight, which does not lend itself in its early stage to either abdominal or rectal palpation. These abscesses may become later on either distinctly iliac or pelvic, or both iliac and pelvic. The second, inferior pelvic, is palpable through the rectum, as it is situated on the rectal wall.

The following statistics give us an idea of the frequency of the pelvic type of abscess. Archibald (2) found among twenty-two cases of appendiceal abscesses that seven were in the pelvis. Rotter (3) found forty pelvic abscesses in one hundred and thirty-two appendiceal abscesses. Of these seven were in the true pelvis and could not be palpated through the abdomen. O. Sprengel collected one hundred and twenty-six cases, of which eleven were pelvic. Hochenegg puts the percentage of pelvic abscess in appendicitis at thirty, which is entirely too high. Hagen's statistics give twelve per cent. In Sonnenberg's collection of one hundred and fifty-six cases there were eighteen abscesses in the small pelvis and six in the pouch of Douglas.

The pelvic and perirectal abscesses are either self-limited by agglutinated loops of bowel and fibrinous adhesions, or communicate with the original abscess. It may be well to mention that in a few cases the sigmoid flexure was interposed between the abscess and the rectal wall, which, of course, constitutes a source of danger in the

event of drainage. A perirectal or pelvic appendiceal abscess may originate either in the course of an acute appendicitis or in many cases develop some time after the onset of the acute process. It is this particular occurrence that demands recognition by the clinician. In our series of four cases the first one developed a perirectal abscess on the twenty-first day, the second one toward the end of the tenth day, the third one on the tenth day, and the last one twelve days after an operation. A perirectal abscess may develop either as a late complication in cases which have not been drained at all, or those which were insufficiently drained, or it may develop in spite of efficient drainage. The histories of our four cases are given below, in brief, and illustrate the clinical and operative course of appendiceal processes complicated by perirectal abscesses.

Case 1. D. C., age 12, Chicago. After an indiscretion in diet the patient was seized with very violent abdominal pains associated with nausea and vomiting, and some rise in temperature. A few hours later when examined she had a definite tenderness in McBurney's zone, a temperature of 101° and a leucocytosis of 24,000. There was considerable pus in the urine. A diagnosis of acute appendicitis was made and confirmed by another clinician. Exploration within twenty-four hours from the time of the onset revealed a mild catarrhal appendicitis. The cæcum, however, was intensely red and œdematous and exhibited a very definite line of demarcation from the colon, very similar to the line of demarcation one finds in gangrene.

The pathology was somewhat unusual, and, not being sufficiently familiar with such a condition, we closed the abdomen without drainage, after removal of the appendix. Following the operation the patient developed very marked vesical symptoms and a septic type of temperature. The general condition of the patient was fair and finding no palpable explanation for this temperature we sent the patient home after sixteen days. The symptoms persisted and for a period of two weeks she ran a strikingly septic temperature. The urine was loaded with pus-cells and the patient developed a very marked suprapubic tenderness. In the course of a week there was a very definitely rounded mass in the median line from the pubis to the umbilicus. Dr. A. J. Ochsner, who was called in consultation, immediately recognized the condition and suggested rectal drainage, which was performed according to his technique. There was a sudden drop in temperature, which had persisted for several weeks, and the patient made an absolute convalescence within a couple of days. There were never any untoward symptoms after that.

Case 2. Mrs. M. P., age 37, Chicago. Was admitted to the Presbyterian Hospital, July 27, 1914, and assigned to my service. She had definite symptoms of appendicitis with marked peritoneal reaction. The usual appendectomy was performed, draining the appendiceal region with two cigarette drains. The appendix was deeply imbedded in adhesions and had a perforation at the tip. The patient did not convalesce well, ran a septic type of temperature, and had marked bladder symptoms. On the basis of the previous experience with the preceding case I made a rectal examination and found a very definite, fluctuating mass on the upper wall of the rectum. The patient was placed in the lithotomy position, the rectum dilated, and the abscess cavity located by inserting an aspirating needle into it. The abscess was drained, the patient making an immediate and absolute recovery.

Case 3. Master I. U., age 3, developed sudden severe abdominal pains, associated with a sudden rise of temperature. For several days the abdominal pains and temperature persisted and, as there was very little localized tenderness or abdominal rigidity, no definite diagnosis was made. On the fourth day of the disease a severe cystitis occurred which masked all symptoms. A rectal examination made on the tenth day, at which time the temperature was in the neighborhood of 104° and the leucocyte count 34,000, a huge perirectal abscess was found on digital examination. The abscess was drained through the rectum and the patient made an absolute and uneventful recovery within two days.

Case 4. A. M., age 16, Chicago, was brought into the hospital with a very well-defined appendicitis. An operation revealed a very acute appendix, with a small abscess cavity which was drained. The patient did very well for eight days. On the ninth day he refused his tray, complained of pain in the lower abdomen, felt nauseated, and had a rise in temperature to 101°. This persisted for a couple of days, during which careful physical examination of the abdomen and chest revealed no findings that could explain this sudden occurrence at this late date. On the twelfth day, we discovered a good sized perirectal abscess, which was promptly drained under gas anæsthesia. After this, the temperature dropped to normal and all symptoms disappeared.

Rectal drainage of appendiceal abscess has its partizans and its opponents. Those who favor the method have obtained striking results and recommend it in males, young females, and children. Oscar H. Allis, Archibald MacLaren, and A. J. Ochsner in this country, Rotter, Morrison, Lange, Jaboulay, Graser, in Europe, favor this method of treatment in selected cases. Archibald MacLaren (4) states: "Many cases of pelvic appendiceal abscesses in men and boys have been opened and drained in both sides, both loins, as well as having suprapubic stabs for large glass or metal tubes, and, in spite of all these different drains, have died of chronic sepsis or amyloid liver because the dependent portions of peritoneum have not been drained." Some of these abscesses if left alone will perforate into the rectum and be cured. In married women all Douglas pouch or perirectal abscesses should be drained through the cul-de-sac into the vagina. Pelvic abscesses have been opened at times by routes other than the rectal or vaginal. Jaboulay (5) employed the parasacral route, Mauclaire (6) and Rotter the perineal route, the latter resorting to it eleven times.

In fairness to the subject I wish to quote John B. Deaver who in his monograph "Appendicitis: Its Diagnosis and Treatment," third edition, page 393, states: "The evacuation of this pelvic variety of peri-appendicular suppuration through the vagina or rectum I regard as opposed to the

dictates of sound surgical practice and as attended by more risks to the patient than the operation through the abdominal wall. By the abdominal route nothing is taken for granted, the field of operation is under the eye, and the appendix can be removed." Deaver further states: "Of all varieties of appendicitis attended by suppuration, these cases of pelvic suppuration due to appendicitis have been, in my hands, among those most successfully treated by operation. The reason for this success is that the general peritoneal cavity can be so thoroughly protected by gauze packs and that in consequence the appendix can be safely removed at the primary operation."

The diagnosis of a pelvic appendiceal abscess can be easily made by rectal palpation. The obligation of a keen clinician, however, is to suspect and foresee this possibility. Any doubtful, acute process of the lower half of the abdomen, particularly in the male, should arouse sufficient suspicion to justify a rectal examination. Cases of acute appendicitis pending for several days or weeks, whether operated upon or not, drained or not, cases which do not go on to convalescence as the average do, should direct our attention to the possibility of a purulent collection situated beyond the region of the appendix. According to Sonnenberg these cases betray their existence by a more or less severe proctitis which sometimes masks the real nature of the trouble. Some cases have more or less severe bladder symptoms.

Rectal drainage as a surgical procedure has the theoretical disadvantage of being an uncertain surgical method, being conducted in the dark, without a distinct knowledge of the tissues involved. Those, however, who have employed the method in cases with a very definite indication for its practice have necessarily become enthusiasts. Oscar H. Allis in a discussion before the Section of Surgery of the College of Physicians of Philadelphia, November 8, 1895, at which John R. Roberts and John C. DaCosta took part, said "he did not defend the operation as one of high-grade scientific surgery, but all his cases got perfectly well and this is better than to have a scientific operation where the patient dies." Our four cases have turned from desperately sick patients into happy convalescents, in every instance, and while we had theoretical scruples and hesitancy in performing this operation, we feel, from a practical standpoint, very much as Allis does. By the way of illustration of the rapidity with which some of these patients recover from an operation of this kind, I wish to quote a case of R. Peterson (7). He opened a large appendiceal abscess which pointed into the rectum and contained a gallon of foul pus. On the sixth day after the rectal drainage the patient walked home, one and a half miles.

The technique employed in our cases was suggested by Dr. A. J. Ochsner. We followed Dr. Ochsner's technique in our first case, which is as follows: The patient is shaved and prepared as for a hæmorrhoid operation. Either gas or ether may be used, although in adults gas is preferable. The patient is placed in the lithotomy position with the buttocks well brought down over the edge of the table. The sphincter is next dilated until it is completely paralyzed. Of course, ether is more suitable for this step than gas. Two long bladed, right angle, flat retractors are next introduced into the rectum, depressing the upper and lower rectal walls. If the diagnosis is correct, the fluctuating mass soon appears in view, being covered by a smooth, shining rectal mucosa. A small incision is made with scissors or knife in the anterior rectal wall and a sharp pointed forceps, dressing forceps, or the blade of scissors is introduced through this buttonhole. The pus generally rushes out with great rapidity, showing that it was held under tension. The evacuation may be assisted by pressing upon the lower abdominal wall. A rubber tube is then inserted high up into the rectum while another one is introduced into the abscess cavity, thus preventing the fæces from entering into it. The tubes are left in place for two or three days and, in our experience, they were always spontaneously expelled. There is practically no after-treatment, except that the bowels are intentionally constipated as after an ordinary hæmorrhoid operation. In the last two cases we have inserted an aspirating needle dipped into lysol prior to the opening of the abscess. Some irrigate the abscess cavity and, on account of adhesions, have no fear of forcing the fluid into the abdominal cavity. There are a number of variations in technique. Some sponge the rectum with alcohol before opening the abscess. The bladder is either previously catheterized or, as Morrison of England does, the catheter is left in place as a guide. Lange dilates the sphincter and removes the fæces dry, so as not to run the risk of having the fluids come down in the course of operation. Jaboulay occasionally unites the lateral wall to the rectum temporarily, so that the upper half drains the abscess while the lower one drains fæces. Some surgeons use Pryor's exaggerated lithotomy position, such as is used for the cystoscopy of the female bladder. One surgeon uses the weighted speculum as used in vaginal work. For drainage some use a simple rubber tube, a

winged tube, or a T-tube. There are certain dangers connected with the performance of this operation. The chief danger, in our mind, is an operation done without any definite indication, in which event needles, scissors, or other instruments are pushed blindly through a septic mucous membrane. An adherent loop of bowel may be injured. The abscess cavity may become infected with stool. In the majority of cases, however, the rectal opening acts as a valve, allowing pus to escape but no stool to get in. A few cases developed a phlegmon of the pelvic floor. Occasionally a secondary hæmorrhage occurs.

CONCLUSIONS

1. Rectal examination is a valuable aid in the diagnosis of acute inflammatory processes of the lower abdomen.

2. A number of cases of acute appendicitis are either associated with or followed later on by pelvic abscesses, some of them pointing into the rectum.

3. Rectal drainage of appendiceal abscesses is a simple procedure and can be resorted to, in emergencies, even by less experienced surgeons.

4. Cases of suppurative appendicitis convalescing badly occasionally do so because the dependent abscess is not drained.

5. In desperate, as well as suitable cases, rectal drainage is a very gratifying procedure.

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SPLANCHNOPTOSIS: A NEW OPERATION FOR GASTROPEXY AND CYSTOPEXY [1]

By J. ALVARADO WALL, M.D., Santiago, Chile

I WISH to give a very short account of a case of abdominal ptosis in which I had the opportunity to perform a gastropexy using a method not yet described which I shall call cystopexy and about which I have found no mention in the literature. The procedure consists, as shown in Fig. 3, in passing three or four sutures from deep in the anterior wall of the stomach up through and fixing them to the peritoneum and fascia in the upper part of the

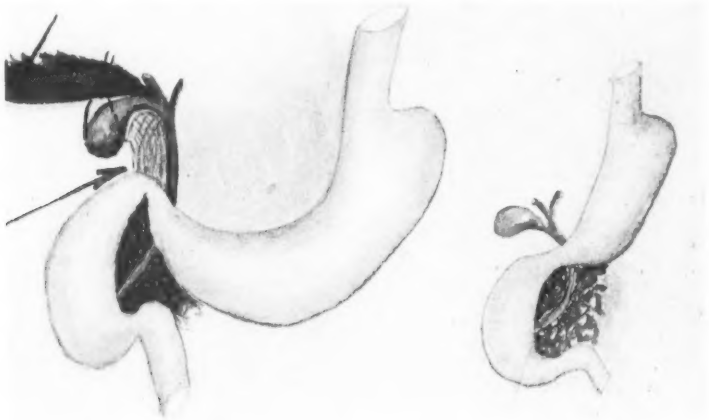


Fig. 1. Condition before operation. Fig. 2. Condition after operation.

[1] Read before the Medical Society of Santiago, Chile.

median incision. In other words it is a method similar to that used by Duret and Rovsing except that it has the advantage of allowing folding in two directions, longitudinally and transversely.

At one of the recent meetings of the Santiago Medical Society, Dr. Benavente, Senior Surgeon to the Hospital San Salvador, called attention to a new fact regarding cholecystostomy. He believes that the separation of the gall-bladder from its hepatic bed is a step of paramount importance in that it allows retraction of this viscus, thus preventing, or at least minimizing, biliary stasis. I am of the opinion that *cystolysis*, as I shall call this procedure, has, in certain cases of ptosis and chronic cholecystitis, a very precise indication. I do not agree with Dr. Benavente as to the mechanism of retraction, for while he believes that the muscular coat is capable of becoming the starting point of active shrinking, I am inclined to attribute the shrinkage to the secondary cicatricial process.

As has already been stated there is not always an indication for this procedure. In my own case it would have been impossible. As careful examination revealed but a fall and increased mobility of the gall-bladder without hepatoptosis, I felt justified in passing a purse-string suture through the superficial layers of the fundus, tying both ends near the anterior border of the liver (Fig. 1).

I do not claim that cases are common in which single cystopexy is sufficient. As a general rule it is necessary to do first a cystolysis and finish with fixation. In this way we correct at the same time the vicious position and the hæmostasis. I refer only to cases of vesicular ptosis not associated with hepatoptosis.

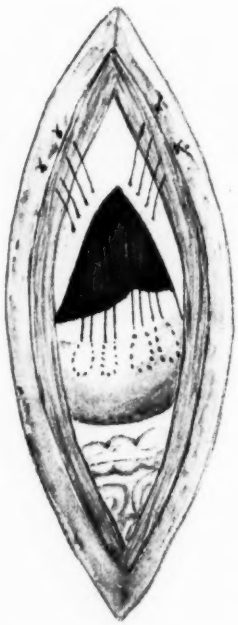


Fig. 3. See text for description.

I am indebted to my friend, Dr. Silva Leon, for his willingness and kindness in drawing the accompanying illustrations.

AN UNUSUAL CASE OF FRACTURE OF THE OLECRANON PROCESS

By C. WINFIELD PERKINS, M.D., New York

MODERN surgeons are more inclined to resort to newer methods of treating fractures, such as grafting, plating, and the different mechanical contrivances for adjusting and setting fractures, than to attempt to adapt the older methods to the more recent means of dealing with these cases. In many instances I believe that with a little aid nature will perform wonders. The following radiograms and history will briefly illustrate what I consider a very interesting and unusual case.

Patient a man of 58 years, fell from a scaffolding and sustained a Colles' fracture of the right arm and a comminuted fracture of the olecranon process of the left arm. Radiograms were immediately taken of both fractures. The Colles' fracture was treated according to the approved methods.

As the fracture of the olecranon was of the variety in which all the fragments were broken into small pieces, the question immediately arose as to what would be the best procedure for treatment. Most authorities recommend incision and replacing the portions of broken bone either by wiring or suture according to the exigencies of the case. Some of the fragments were so small that it seemed best to advise their removal and adjust the remaining large fragment of the olecranon in place as near as possible to its original position. However, conservatism prevailed and it was decided not to do an open operation but to wait and see what nature would do, and if an operation were necessary it could be done later.

The patient was therefore anæsthetized, the arm put in extension, and an effort made to align the fragments and place the remaining portion of the olecranon in as near as possible its original position over the trochlear surface of the lower end of the humerus.

Adhesive strips and a gauze pad together with a wire splint were finally placed on the elbow. In ten days' time the splint was removed and the arm put in the first degree of flexion. Passive motion was instituted at the same time. In seven weeks' time the patient made an almost perfect recovery as regards function of the joint.

Radiogram (Fig. 1.) illustrates the fracture immediately after the injury. Fig. 2, ten days afterward, shows alignment of the fragments and partial regeneration of the olecranon process. Figure 3 illustrates the entire new olecranon process formed. At the time the last radiogram was taken, there was good motion to the joint with slight limitation of extreme extension.

I am indebted to Dr. F. H. Goddard of Rochester, New York, for the radiograms that accompany this sketch.

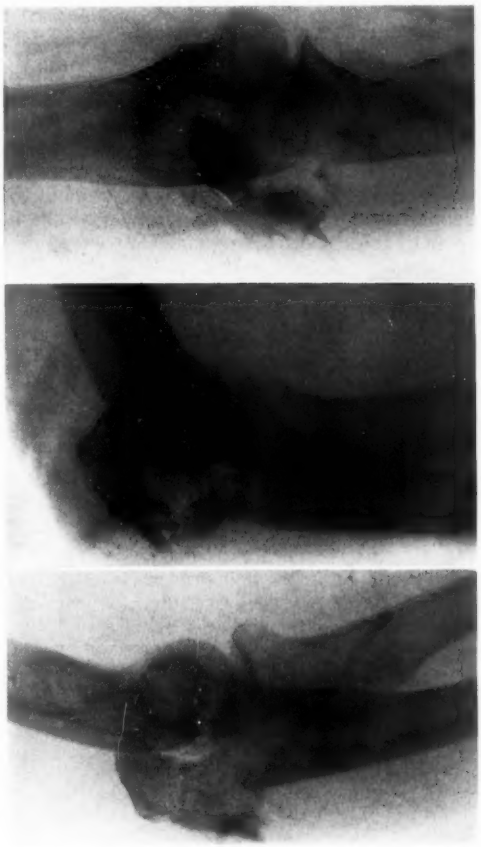


Fig. 1. Radiogram immediately after operation.
Fig. 2. Radiogram of fracture ten days after fracture. Note alignment of the fragments.
Fig. 3. Radiogram showing entire new olecranon process.

ROENTGENOLOGIC DIAGNOSIS OF PROSTATIC TUBERCULOSIS AND PROSTATIC STONES

By MAX REICHMANN, M.D., Chicago

CONTRARY to Socin[1] who in his monograph "Diseases of the Prostate" claimed that tuberculosis of the prostate is an extremely rare occurrence, all authors of today are agreed that the affliction is quite common.

In most cases of genito-urinary tuberculosis the prostate is also infected and Huter even states that genito-urinary tuberculosis originates in the gland. Of course, this is going too far; but there are in the literature numerous cases to be found where the initial tuberculous focus was located in the prostate. Most cases undoubtedly are infected from a diseased epididymis, quite a few from tuberculous kidneys or seminal vesicles. Baumgarten maintains that a descending infection with Koch's bacilli affects the urinary organs only, while an ascending infection confines itself to the sexual organs.

The pathology can be shortly described by the appearance of disseminated nodules which have the tendency to conglomerate; they are transformed into caseous masses, indurated connective tissue, and finally into calcification.

From the roentgenological standpoint this final development is of great interest, because in this stadium we are able to make the diagnosis from the characteristic appearance of the plate alone, as the following case will show.

[1] Billroth's Handbuch, 1875.

I am deeply indebted to Dr. W. T. Belfield for the following history:

K., age 46, married twenty years, wife never pregnant, acquired lues 25 years ago, and had specific treatment for the same for several years; general health good, aside from vesicle irritation, for which he consulted Dr. Belfield January 11, 1915.

This irritation, marked by frequent urination; diurnal and nocturnal alike was first noticed over twenty years ago, some months after apparent recovery from gonorrhœa. For some ten years his frequent micturation was intermittent, being sometimes unnoticed for several months. During the past eight years, however, it has been continuous and has been steadily aggravated.

Present state. Well nourished, active man; no complaints except micturation every hour or less, day and night.

Urine voided contains many pus-cells, also blood, staphylococci, and streptococci. No tubercle bacilli detected. Left epididymis vesicle and both sides of prostate nodulous; some tenderness but no swelling over left kidney. Urethral stricture stopping No. 21 F. at sound at bulbomembranous junction. Sixty ccm. of residual urine in the bladder. Wassermann negative, temperature 99.8° (2 o'clock p.m.).

Injection of ¼ milligram old tuberculin was followed by pronounced general, local, and focal reactions. Treatment has consisted, aside from gradual dilatation of stricture, of gradually increasing doses of bacillary emulsion of tuberculin, and tonics.

Within four months the nocturnal urinations decreased from 7 to 8 to 1 to 2 each night, the diurnal intervals lengthened from 30 to 40 minutes to 2½ to 3½ hours. Two tuberculous ulcers in the trigonum healed.

The fact that there still remained some urinary fre-

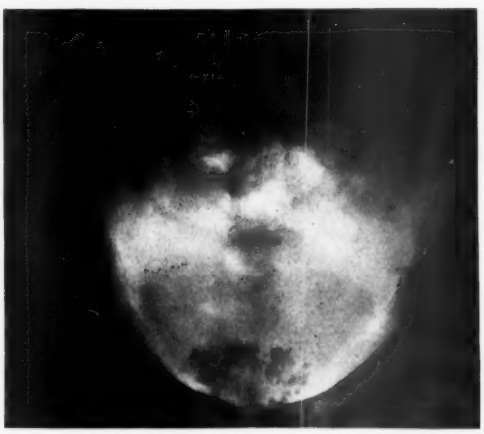


Fig. 1. See text for description.

Fig. 2. See text for description.

quency and pus—contrary to Dr. Belfield's usual observation of such cases treated with tuberculin — led the doctor to suspect calculous deposits beyond the range of the cystoscope. To determine this question he was referred to me July 24, 1915, for roentgen examination.

The plate (Fig. 1) showed the same condition as did a few plates I have made of cases of tuberculous kidneys and therefore without knowing anything about the history and the clinical findings of the case, I reported to Dr. Belfield that we had to deal with a case of tuberculosis of the prostate, a diagnosis which the doctor confirmed.

As far as my knowledge of the literature, American and foreign, goes, this is the only case in which a positive diagnosis of secondary prostatic tuberculosis was made from the roentgen examination alone. As far as differential diagnosis is concerned there is only one condition of the prostate which roentgenologically comes into consideration; i.e., calculi of the prostate.

One glance at Fig. 2 will enable the experienced observer to differentiate between the two conditions. The shadows of the always multiplex stones lay close together; in fact, if the technique is faulty one may diagnose only one stone present.

Roentgenographic diagnosis of stones in the prostate has been reported a few times. Goldin-Bird[1] was the first to publish such a roentgenogram, and Frisch in his handbook maintains that stones in the prostatic gland which are deeply imbedded in the parenchyma of the gland, can never be detected except by roentgenography

[1] Brit. M. J., 1898.

COMBINATION NEEDLE HOLDER AND LIGATURE SCISSORS[1]

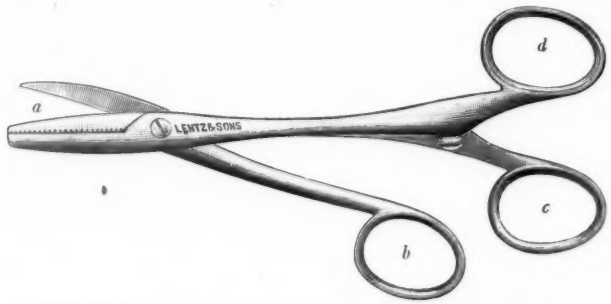
By LEVER F. STEWART, M.D., Clearfield, Pennsylvania
Surgeon to the Clearfield Hospital

THE accompanying cut shows a combination ligature scissors and needle holder which I have used in my clinic during the last nine months with complete satisfaction.

Prior to the manufacture of this instrument under my direction by an instrument house in Philadelphia, it had been my custom when placing sutures to hold a pair of scissors in thumb and little finger and a Deaver needle holder in the thumb and ring finger of the same hand on top of the scissors. This way of working afforded considerable speed but was cumbersome.

The instrument I am about to describe has all of the advantages of the Deaver needle holder, after which the needle holder portion is modeled, and in addition it enables one by bringing the middle finger into play to make use of scissors. Obviously such an instrument is convenient and time-saving.

Briefly, this instrument shows the needle-holder jaw that is superior when the holder is properly held in the right hand, to have a cutting edge that is slightly curved on the flat. This cutting edge is on the side of the jaw that would lie inferiorly when the right hand is rotated to the right. The other addition to the instrument is a scissor blade that fits the jaw blade in contour and has a shank with a finger holder that terminates just anterior to the finger holder of the needle-holder shank which accommodates the ring finger. In this way the middle finger fits easily in the finger holder of the scissor shank and



Combination needle holder and ligature scissors for use in right hand, *a*, scissor edge of holder jaw, *b*, scissor shank for middle finger, *c* for ring finger, *d*, for thumb.

[1] Submitted for publication October 19, 1916

the operation of the scissors is carried out by the use of this finger after first locking the shanks of the needle holder by forcing them together. The scissor shank has a separate screw lock just anterior to the screw lock of the needle holder. Some bending of the scissor shank was necessary in order to bring the finger holder into the desired position.

The cutting edge and curve on the flat of the holder jaw do not affect its strength. The end of the jaw is kept blunt and the scissor portion is not designed to reach the furthermost end of the jaw. This with the scissors curved on the flat in addition, makes little likelihood of cutting any other structures when cutting ligatures. Furthermore its construction prevents the cutting of ligatures too short. I would add that the scissor blade is not made of a width sufficient to interfere with any needle held in the jaw of the holder.

This instrument is in no way more cumbersome or less serviceable than the ordinary Deaver needle holder. In fact the additional holder for the middle finger enables one to operate the needle holder portion with greater ease.

The bringing of the scissor portion into play requires a bit of sympathy with this method of working and a slight amount of practice. Its perfection means the saving of time when placing sutures (especially interrupted ones), and ligatures when it is necessary to use a suture.

This instrument would of course be of no advantage to a surgeon who leaves the cutting of sutures and ligatures to an assistant who would have less knowledge of the site to cut and must therefore be less perfect than the operator in this capacity.

The scissor blades have remained sharp as long as scissors ordinarily do and though not designed for it, will if necessary cut tissue; however they are not as satisfactory for this as ordinary scissors.

The instrument can be used in either hand though it is more satisfactory for one who is ambidextrous to have an instrument made for each hand, with one instrument having the shanks arranged for right and one for left hand use (see illustration).

To summarize: The instrument described has all of the advantages of the Deaver needle holder when used as such and in addition affords an entirely satisfactory ligature scissors without the inconvenience of either holding two instruments in the hand or laying one instrument down and picking up the other.

While still holding the instrument suture tying can be done without inconvenience.

PLACENTA PRÆVIA TREATED WITH PITUITARY EXTRACT

Report of Cases

By PAUL GALLAGHER, M.D., El Paso, Texas, and HIRAM GALLAGHER, A.B., M.D., Los Angeles, California

FROM the beginning of the practice of obstetrics, placenta prævia has been the complication most dreaded by the accoucher. Not only has it been most dreaded, but it has been accepted in a spirit of almost total hopelessness for the child. From the time of Barnes (1) who gave us the first accurate description, or almost from that of Portal (2), in 1685, and Schacher (3), in 1709, the subject of placenta prævia has been *in statu quo*. Maternal mortality varied from 1 per cent to 4.5 per cent, and, fluctuating with the series, fœtal mortality was from 35 to 61 per cent, with the further expectation that fully 50 per cent of the children born alive, would die within the first ten days. This was a pretty hopeless outlook, particularly as we had come to believe that the chance for the mother decreased directly with our efforts for the child. It was stated by Williams (4) that fœtal mortality is not susceptible of any material reduction, for the reason that the pregnancy is generally terminated before term, when the chances for extra-uterine life are relatively unfavorable.

The outlook has of late given way to a much more optimistic one. The advent of pituitary extract and its use in obstetrics is, in the opinion of the most recent writers on the subject, a decided step in advance. Certain practitioners feel that perhaps here is an agent which will help take from placenta prævia its present unfavorable and dangerous aspects. Among the recent observers of the results of the pituitary extract practically Hamm (5) only, anticipates trouble from the use of the drug, and that because of his unfortunate experiences when induc-

ing labor prematurely. No other observer seems to have had the trouble which he reports of the formation of stricture in the lower uterine segment, and all seem to think pituitary extract, in the treatment of placenta prævia, the agent of choice.

The drug has been used in the treatment of 4 cases in my own work and it has proved of inestimable value. I have used several of the preparations on the market, all put up in ampouls, sometimes using two or more preparations in a single case. The results were uniformly good. The treatment was effective in all of the cases which is contrary to the results reported by Jacoby (6). However, its ineffectiveness should not be seriously apprehended since our position in that case could be no worse than before.

Vogt (7) says that experiences have been too few to give accurate indications as to the use of the drug, but he quotes Hofbauer (10), whose opinion concerning it is decidedly favorable. He cites one case in which rapid delivery caused a cervical tear through the entire wall of the uterus, with rupture of the uterine artery. This may have been due to large doses given too early. However, this case is the only one of the kind reported in a literature already becoming voluminous, and, without in any way dissuading us from the use of the drug, the incident has served to make us more guarded. Notwithstanding the fact that numerous "accident-less" cases are reported, the accident might happen again.

Sachs (8) has reported 16 cases. In 4 the results were good, in 4 fair, and in 4 bad. In the last 4 the pains had not begun when the drug was given. This seems to me a decided contra-indication, since the extract cannot be expected to initiate labor. Sachs further states that a slightly dilated cervix is a contra-indication. In discussing the extract, he gives placenta prævia as one of the indications for its use.

Puppel (9) advocates the use of the extract in combination with version. Hofbauer (10) speaks of its excellent service in placenta prævia, but adds that if half or more of the orifice is covered by placental tissue, he does a metreurysis or combined version first. Hirsch (11) contributes a valuable point in touching on the need of several injections. One large dose cannot afford as good results as several small doses judiciously repeated. However, the time consumed in Hirsch's series, from 3 to 6 hours, seems to me too long and too fraught with the danger of bringing the method into disrepute by unfavorable results. I believe the time in his series could have been shortened with perfect safety and with more satisfactory results if the doses had been a little more frequent and a larger dose had been employed when the cervix became easily dilatable or when dilatation was complete.

Hauch and Meyer (12) report among 6 others, one very successful case in which, besides placenta prævia, there was a prolapse of the cord with a very low insertion (3 cm. from where the membranes were torn) in a delivery three weeks before term. Four of the other cases were successful, 2 of placenta prævia totalis were failures. Failure due to inactivity, maternal or medicinal, is described by Jacoby (6) only, who reports also one successful case.

Fuchs (13) and Fournier (14) report favorable results; the latter of whom details a case in which the extract was not used until two and one-half hours after the first very severe hæmorrhage. Nevertheless, successful delivery was accomplished seven and one-half hours after the beginning of labor.

The articles written by Gall (15) show his optimism and give the greatest hope for future development of the technique and the results. He says that results have been so good as to warrant further use of the drug. Out of 10 cases of placenta prævia centralis, all the mothers except one who was moribund when first seen, were saved. The fœtal mortality in his cases was high but was explainable and did not reflect on the treatment. In these cases the fœtal heart sounds were not distinguishable on the admission of the mother to the hospital. He believes the treatment best for both mother and child. No tears of the cervix nor any uterine strictures were noted in his series of cases.

Fischer (16) and Studeny (17) report results which amply justify for them this mode of treatment. Madill and Allan (18) combine the use of the extract with version, and Oria (19) with the use of Charpentrier bags. In view of the other reports, however, this latter seems somewhat unnecessary.

Without citing any cases Quigley (20) gives placenta prævia lateralis as an indication for the use of pituitary extract. Trapl (21) has reported 16 cases with 3 stillborn infants. However, two were dead before the treatment was begun. The one death was unexplained, occurring 4 hours after the beginning of treatment. Trapl does not believe it was due to the extract, since he noted an increase in heart sounds after the beginning of treatment. He has moreover seen a living child delivered several hours after the sounds had become weak and irregular. He recommends that the extract be given regularly and be repeated if needed.

Druskin (22) cites two cases without comment. In one there was a good result for both mother and child and in the other a stillborn child. Anderson (23), in a discussion of pituitary extract, gives placenta prævia as an indication for its use. He quotes an early paper of Vogt (7) which recounts the successful results of its use in 7 cases.

Stratz (24) has stated in a recent paper that the child mortality in his cases without the use of the extract, is 45 per cent, while statistics for the whole Netherlands show 43 per cent for children and 7 per cent for mothers without the use of the extract, and according to the old methods of treatment. It seems to me that no greater argument could be offered for the use of pituitary extract in placenta prævia than Stratz's paper with its appalling statistics, as compared with the worst recounted under the new method of treatment.

The following are brief histories of my own cases:

CASE 1. M. A., age 30, V-para, married 8 years. *Examination at term.* The patient was bleeding freely, the os dilated to about the size of a quarter-dollar; marginal placenta prævia, to the left side; position could not be diagnosed, but the head was well down. At 11 p.m. pituitary extract was administered (½ cm.). The pain increased and the bleeding became less. At 12:00 m., the dilatation and bleeding were increasing. One-half cm. of the extract was given. At 12:30 a.m. there was less bleeding. At 1:00 a.m. dilatation and bleeding were increasing, and the membranes were ruptured. One cm. extract was given. Very rapid delivery in the occiptolævo-anterior position. The placenta was delivered in two parts; first, the size of palm; second, cord membranes, etc. The condition was satisfactory. At the end of 6 months, the mother and child were both well.

CASE 2. J. M. de G., age 30, IV-para, married 8 years. Pains began at 10 p.m. At 12:00 m. the patient was bleeding freely with pains about the same. Presentation and position were occipitolævo-anterior. Right marginal placenta prævia, ½ inch. Fœtal heart-sounds indistinct. ½ cm. pituitary extract was given. At 12:30 a.m. bleeding was the same. Dilatation about the size of a half-dollar. Pituitary extract ½ cm. At 12:45 a.m. bleeding was less, pains more severe; head descending well. At 1:15 a.m. there was dilatation about the size of a silver dollar. Bleeding was about the same. The membranes were ruptured. One cm. pituitary extract was given. Satisfactory delivery at 1:30. Infant slightly apnœc. At the termination of my visits, which was the last time I saw either, both mother and child were well.

CASE 3. F. G. de E., age 24, married 7 years. Presentation and position occipitolævoposterior. The fœtal heart sounds were very plain. The patient was examined one hour after the beginning of mild pains. There was some oozing. Left, marginal, placenta prævia. Gradual progress of pain and bleeding to severe bleeding. At 8:00 p.m. ½ cm. of pituitary extract was given. At 8:10 p.m. bleeding less and pains were more severe. At 8:30 p.m. pains were very stormy. At 9:00 p.m. pains were less, bleeding more severe. Dilatation was about the size of silver dollar. Patient given 1 cm. of pituitary extract. At 9:15 p.m. satisfactory delivery in membranes. Small child. Both mother and child well when last seen about a year later.

CASE 4. L. A. de F., age 29, VIII-para, married 14 years. Upon examination no fœtal heart sounds could be detected. Presentation and position occipitolævo-anterior. The pains were weak. Placenta prævia overlapping left side. At 8:00 p.m. dilatation was about the size of quarter dollar. The patient was bleeding freely. She was given ½ cm. of extract. At 8:30 p.m. dilatation was about the size of half-dollar. The bleeding was less. At 9 p.m. dilatation and bleeding were increasing. She was given ½ cm. of pituitary extract. At 9:30 p.m. dilatation was proceeding. The bleeding was severe. The membranes were ruptured. One cm. of pituitary extract was given. At 9:40 p.m. expulsive delivery. The child was stillborn. About twelve months later the patient was delivered by a midwife of another child. Both are now well.

SUMMARY

For the treatment of placenta prævia in general I would recommend:

1. That everything be in readiness to do a version or metreurysis if necessary.

2. Pituitary extract should be used in small doses (½ cm.) repeated as needed during the latter part of the first stage, and followed finally by a large dose (1 to 1½ cm.) when the dilatation is complete.

3. Restrain impatience as regards the progress of the case but be advised minutely as to the presenting part and the condition of the mother in order to be ready for instantaneous interference when it is warranted.

4. Be prepared for emergencies which may require interference.

5. Be prepared for giving an intravenous saline in case of extreme loss of blood. The reduction of pressure consequent on the loss of blood, often kills these patients, and an intravenous infusion can be given even while parturition is in progress.

6. Be superlatively aseptic. It is my opinion that the relative rarity of infections in these cases is largely due to a "local parturition immunity" arising from the œdema and swelling with the cofferdaming of the tissue spaces. However, this does not warrant any varying from the strictest aseptic practice. While parturition is a physiological act every delivery is a surgical case in which the surgical work is carried on under the most adverse circumstances. Particularly is this true in placenta prævia and for this reason more care and more rigid asepsis should be the aim of every accoucher.

With the limited number of cases I have treated the results can hardly be considered authoritative, but they have been so exceedingly good that I have deemed it advisable to make this report for the benefit of those who may not have inves-

tigated the literature on the subject, or who for fear of possible consequences, may be meeting the condition of placenta prævia with the old apprehensions and the old method of treatment.

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THE TREATMENT OF FEMORAL ANEURISM

By FREDERICK G. DYAS, M.D., F.A.C.S., Chicago

THE purpose of this paper is to bring out some points in connection with the treatment of femoral aneurism which appear to be overlooked by many writers.

The time of operation is an all-important consideration because if sufficient time be allowed to elapse between the date of the appearance of the aneurism and the operation, in most cases a sufficient collateral circulation will have been established to permit of the tying-off of the vessel if the aneurism be below the point at which the profunda femoris is given off. Dr. James Neff, in an article published two years ago in Surgery, Gynecology and Obstetrics, demonstrated the use of an arterial clamp which gradually occludes the lumen of the vessel, thereby permitting time for the establishment of the collateral circulation. The importance of the element of time cannot be exaggerated, for upon the collateral circulation depends the life of the limb or even of the patient himself.

During this period of waiting for the establishment of the collateral circulation the patient should be kept absolutely in bed because of the danger of rupture of the aneurismal sac and, secondly, because the further development of the aneurism is best retarded by rest.

The second important consideration in the treatment of femoral aneurism is the location. If the aneurism be situated above the point at which the profunda femoris is given off the condition is very greatly complicated. However, most writers agree that if the circulation be retained in the deep femoral artery the superficial vessel may be safely ligated.

Third, the choice of operation is not always left to the discretion of the operator, because the pressure in the femoral artery is high and the

conditions for plastic work are far less ideal than in smaller vessels.

Aneurisms of the femoral artery are almost always caused by trauma, contrary to the development of these lesions elsewhere, which are so frequently brought about by specific infection and arterial disease. In the cases of femoral aneurisms seen in the past two years at the County Hospital all have been caused by gunshot wounds, the tendency being for the victim to endeavor to shield himself by turning sidewise toward the bullet. In most cases the bullet has just grazed the thigh, or else penetrated the deep muscles and wounded the adventitia. The aneurism, of course, may also be caused by stab wounds, but this is rare.

The dissecting aneurism is the type most commonly produced; rarely the spindle-shaped tumor which is observed as the result of luetic infection. The heavy muscles of the thigh are raised up and frequently to some extent separated if the condition persists for any length of time. The patient complains of great pain which is worse when he exercises and necessitates frequent stops in attempting to walk. There is frequently cyanosis of the extremity and the temperature of the limb is lowered. The patient finally becomes entirely incapacitated for work and rapidly loses weight and strength because of his inability to sleep on account of the pain.

The case herewith reported is that of a Mexican aged 27 years who about sixteen months previous to operation was shot from the front, in the region of the left Scarpa's triangle. There was very little hæmorrhage at the time; he could walk afterward but he suffered pain in the wound and remained more or less in his bed for two months. After this he had no trouble whatsoever, but there was no impairment of function in the left leg or hip. However, pain began in the same area five weeks before operation, with no injury just before. The pain came on gradually, was always pounding or throbbing in character and grew gradually worse. Soon after the pain began, a small swelling was noticed in the same area and this swelling increased gradually as the pain grew worse. Movement of the left thigh was impaired because of the pain and swelling, and the pain usually was referred down the inner thigh to the knee.

Examination revealed a tumor in the upper, inner aspect of the left thigh, semispherical in shape, with a distinct, visible, heaving, expansile pulsation synchronous with the heart beat. Expansile pulsation was easily palpable; there was a marked systolic thrill felt over the tumor on its lateral border near the region of the femoral artery. The mass was dull to percussion, felt hard but elastic, could be indented by pressure and was not very movable. There was a marked systolic bruit over the entire tumor and above and below the tumor for variable distances. It was most marked over the lateral border of the tumor, the entrance and exit wounds of bullet shot of last year. The hip-joints and knee-joints were normal, motion was unimpaired, and there was no pain. The patient walked to the ward. The femoral pulse was delayed on the left side and slower in returning in comparison with the femoral above the pulsating mass.

Pathology. The aneurism was about the size of a large apple, situated just below Poupart's ligament and extending down about one-third the distance of the thigh. There was a very marked heaving, expansile throb together with a loud bruit. The aneurism had lifted up all the tissues above it and was causing the patient great pain. It has been increasing rapidly in size for the past month.

Operation. Operation was performed on June 11, 1915, at Cook County Hospital. A long incision was made from about the level of the umbilicus on the affected side downward over the course of the femoral artery as low down as the level of the patella. The abdomen was first opened, the peritoneum pushed up out of the way and a provisional ligature put around the external iliac artery. The common femoral artery was exposed just below Poupart's ligament and a provisional ligature carried around it by means of an aneurism needle, carefully pushing the femoral vein out of the way. At this point it was discovered that the aneurism came off the superficial femoral artery at a point one-half inch below the point of origin of the profunda femoris. A double ligature was now placed around the superficial femoral at just the point where the profunda was given off and a protective clamp was placed around the artery just above the aneurism.

The soft parts were now carefully dissected from the aneurismal sac and an effort made to isolate the distal portion of the femoral artery guided by the sartorius muscle at the point of emergence of the femoral artery at the opening in the adductor magnus muscle. It was found impossible to locate the artery below the aneurism so the aneurismal sac was opened. This contained a large quantity of fresh arterial blood and also black, clotted blood, which was carefully scraped out. Bleeding occurred from the distal portion of the artery at this time, which was identified by means of the hæmorrhage. This was doubly ligated, close to the sac leaving the field quite dry. Only a small portion of the aneurismal sac was removed. The remainder was top sewed and left in place. No attempt was made at plastic work because the circulation remained good after the tying of the superficial femoral artery, as was evidenced by the bleeding from the distal portion and also by the fact that the femoral vein was quite full. The patient's foot and leg remained warm and he left the operating room with a pulse of 120.

The wound healed by primary union and the stitches were removed on the tenth day. The patient was allowed to walk about at the end of that time and left the hospital at the end of three weeks with perfect function in the affected extremity. The temperature of both feet was equal and there was no discomfort of any kind. To all intents and purposes he made a complete recovery.

CONCLUSIONS

1. It is advisable to allow ten days to two weeks to elapse between the time of injury and the date of operation.

2. Double ligation is the best method in aneurisms in this position. Great care must be exercised to ligate the distal portion after the collateral circulation is formed or severe hæmorrhage will result.

3. The ultimate results of this type of treatment are good.

CORRESPONDENCE

FRACTURE OF THE NECK OF THE FEMUR

To the Editor: I have read with pleasure and profit the paper by Dr. McGlannan on "Fracture of the Neck of the Femur," in the March issue.

I note with particular interest that 20 patients were treated by the abduction method with but one death; that in the remaining 19 bony union followed; and that the investigation of final results (from 9 months to 8 years afterward) in the cases available for examination (11 in number), showed 9 good results, or 80 per cent, which is quite out of comparison with any others that have been reported.

This record is of especial importance because it proves that fracture of the neck of the femur may be treated on surgical principles; namely, by immediate reduction of the deformity and by secure fixation of the fragments, and that the results, as in other fractures, are dependent upon the character and quality of the treatment.

In the description of the abduction method, Dr. McGlannon states that after the reduction of the deformity, the limb is placed in full abduction and slight flexion, that the other thigh is included in the plaster for security, and that a pad is placed behind the trochanter to assure inward rotation. This is not quite correct. The limb is placed in complete abduction and complete (hyper) extension; the other thigh is not included in the support, nor is a pad placed beneath the trochanter. Complete extension as contrasted with flexion increases the tension on the capsule which is the basis of security and prevents a sagging backward of the shaft fragment if the plaster spica becomes loose. The sound thigh is not fixed because to do so adds a burden and restraint which is unnecessary if the plaster is properly applied.

I am at a loss to understand how, in the face of the results of his investigation, Dr. McGlannan finds it necessary to describe at length a method of traction by ice tongs imbedded in the femur, a modification of traction by the Steinmann nail—a method which has all the disadvantages of ordinary traction; i.e. elevation of the foot of the bed, persistent pressure on the buttocks, uncertainty of reduction and control, with the very doubtful advantage of a more direct pull with the limb in an attitude of flexion.

The same criticism may be made of the treatment in Class F, in which the thighs are abducted on a spreader, which is attached to the bed rail, and in which, by elevating the foot of the bed the traction of the body is supposed to reduce deformity and to assure subsequent security.

Traction treatment, of whatever type, is mechanically defective as a means of assuring the essentials of success. It has the further disadvantages of compelling rest, if not on the back, at least on the buttocks, where pressure is concentrated; usually with elevation of the foot of the bed. These disadvantages can hardly be compensated for by the occasional assumption of the sitting posture as a preventive of hypostatic congestion.

The abduction method is complete in itself. The head of the bed may be raised to any degree, and the patient may be moved at will and turned completely over without discomfort. There can be, therefore, no danger of hypostatic congestion, and bed sores, which are almost unavoidable under ordinary conditions, need never occur.

A comparison of the results of the abduction method, already referred to above, and those treated by the alternative methods described, is of interest. Of 9 patients, 2 died under treatment. In 3 cases the time was too short for report, and of the 4 others, 1 may be classed as a good result, although with a "rigid hip" (25 per cent).

The abduction treatment has been many times described during the past 14 years, yet at the present time it is not properly presented in any of the special treatises on fractures; consequently, its principles and its proper application are not usually understood by those who criticise it. Those who may wish to consult the original source may find one of the more recent descriptions in the *Annals of Surgery* for October, 1914.

ROYAL WHITMAN, M. D.

New York.

TRANSACTIONS OF SOCIETIES

CHICAGO SURGICAL SOCIETY

REGULAR MEETING HELD JANUARY 7, 1916, WITH THE PRESIDENT, DR. S. C. PLUMMER, IN THE CHAIR

RECONSTRUCTION OF THE PYLORUS

DR. ALFRED A. STRAUSS: I want to show a method by which I have dissected one-half of the pylorus and tried to reconstruct it with two superimposed fascial transplants. I have been impressed with the results that have followed this operation. The best results from gastric ulcer are in those cases in which resection of the ulcer can be made without gastro-enterostomy, and the question arose, could not the same principle be applied to the pylorus, provided there is some means of reconstructing its lumen. Considering the question from that standpoint I undertook an experimental study in trying to reconstruct the pylorus. Because of cicatrization of the pylorus in those cases in which the Heinecke-Mikulicz pyloroplasty is done the results are not satisfactory. There is some scar formation and usually a dilated stomach with its obstructive symptoms. Instead of this operation, I supply a fascial transplant, by which the pylorus is quite easily enlarged to its normal size and lumen.

POST-OPERATIVE TETANUS

DR. KELLOGG SPEED read a paper entitled "Post-operative Tetanus." (See p. 443.)

DISCUSSION

DR. JOHN F. GOLDEN: To Dr. Speed's paper I can add a report of one case with deductions drawn from it.

In the first place, the treatment of tetanus is prophylaxis. After tetanus begins, I believe there is a consensus of opinion at the present time that there really is no efficacious saving treatment; that efficacious saving treatment is only the prophylactic treatment. The prophylactic and saving treatment of some of our cases of post-operative tetanus, due to my experience with the case I am about to relate, is in determining what the cause of the tetanus is, whether it is from the intestinal contents or from the catgut used at the time of the operation. If tetanus develops in a particular case from the catgut, it seems to me we can save the other cases that were operated on at the same time by giving all of them prophylactic treatment and by stopping the use of that particular catgut, or giving prophylactic treatment to the cases we immediately operate on.

Some two or three years ago, when Dr. Murphy left for a trip to Europe, I had the usual number of post-operative cases to look after. At that time I believe there were about ninety. Some of them were recently operated on. About two days after Dr. Murphy left one of my associates reported that one of the patients was having an attack of hysteria. I did not go over to the hospital immediately, but subsequently on making the rounds I came to this patient. She had a locking of the jaw but no temperature. She had been operated on some five days before, and while she had only this locking of the jaw I made a diagnosis of tetanus. I telephoned the doctor who referred her to me, stating that his patient had tetanus and was going to die and, if possible, to come to the hospital. The patient, five and one-half days after the operation, had this locking of the jaw. The last seven hours of the first twelve we watched the patient very carefully. I had consultations with older men in the case, and my diagnosis was not concurred in. The patient died at the end of twenty-four hours, six and one-half days after the operation. I attributed her condition to infection from within the alimentary canal. The operation was a simple one. I did not give the cases that were operated on that same day (there were five or six of them) a prophylactic dose of antitetanic serum. I went on operating that day and daily afterward without giving these patients antitetanic serum and used the same catgut. Some two or three weeks after Dr. Murphy's return he received in his mail a letter from a surgeon in Calcutta, India, warning him that the catgut he was using, was the cause of tetanus in cases in India. Dr. Murphy looked the matter up and the catgut used in this particular case I have quoted was manufactured and sent out at the same time as the catgut that was used in Calcutta, India.

The prophylactic treatment, while, of course, not always efficacious, is generally so. We have had no case in which we have used antitetanic serum. It is the only efficacious treatment we have, and therefore when our cases develop post-operative

tetanus attributed to the use of catgut, we use only prophylactic treatment.

This is the only case I have had experience with, and it has taught me that it would have been a good thing to have given prophylactic treatment to the cases that were operated on at that time and to have changed the catgut on the cases which I continued to operate on in Dr. Murphy's absence.

DR. ROGER T. VAUGHAN: On November 2, 1915, a boy, six years of age, came to the Cook County Hospital in the service of Dr. Besley, with extensive injuries of the right leg and left groin, the result of being run over by a vehicle. The skin was stripped from his right leg most of the way from the ankle to the groin, and the sewing up of the wound was quite an extensive procedure. The fascia was exposed and, in places, the muscle, too. I was called to help the interne sew up the wound in the operating room. We mopped out the wound thoroughly with iodine and cut away all severely crushed and non-bleeding tissue, especially that with dirt ground in it. The next day the boy was given a prophylactic dose of antitoxin, fifteen hundred units. The following noon, November 4, the patient had a few convulsive twitchings in both arms, and these continued throughout that afternoon. Whether there was trismus or not, was a matter of dispute among those who saw him. I was not there that day, so I have to accept the report of others. At any rate, it was considered a case of tetanus by one of the doctors, and the two others who doubted this diagnosis because of the slight trismus and the unusual distribution of the convulsive movements, were unable to suggest a diagnosis of their own.

At first only some dead skin was cut away; but the convulsive twitchings in the arms becoming more frequent, finally under gas anæsthesia amputation near the hip was performed, and shortly after this operation the patient died. The indication for operation was not only the suspected tetanus but also extensive discoloration of the leg which was believed to be the expression of an impending gangrene.

I have not run across any case of tetanus of only two days incubation period, and I should like to ask Dr. Speed if he knows of any such cases or if he has seen any go on to so early a fatal termination in spite of prophylactic injection of antitoxin. Traumatic fat embolism was considered, but the onset of the symptoms seemed rather too late for that condition.

Not long ago in Cook County Hospital we had one post-operative tetanus case in a child. It came on two weeks after circumcision was performed, and the sutures used were not catgut but horsehair. We took specimens of the horsehair from the dressing room where the operation had been performed and from other dressing rooms and no tetanus bacilli were found in any of the samples. That boy recovered.

I saw another case of post-operative tetanus at the County Hospital six or eight months ago which developed in the gynecological service six or seven days after an extensive repair of pelvic adhesions and went on to a fatal termination within 12 hours of the onset of symptoms. On that same day in the operating room, using the same catgut, seven or eight other operations were performed and this was the only case of tetanus that developed; and no cases have developed since then to my knowledge.

DR. DEAN LEWIS: I would like to ask Dr. Speed if in any of these cases he knows whether the spasms developed around the seat of the injury and if they were near also the point of infection? It is now recognized that trismus and spasm are the late symptoms of tetanus rather than the early ones.

I have not had any experience with post-operative tetanus, but I have seen one case which developed about sixteen days after an injury to the foot in which the spasms were limited to the nerve supply, or to the muscles supplied by nerves at the point of distribution about the site of the injury without any general spasm or trismus developing. So I would like to ask the doctor if in these cases he has seen them early enough to say whether there was local spasm which would give a clue to the site of infection.

DR. E. WYLLYS ANDREWS: The whole interest of this paper lies in the possibilities it opens up as to carriers in human beings who are subject, after intestinal or stomach operations, to tetanic infection. I would not have believed it possible, *a priori* but one of these six cases reported by Dr. Speed occurred in my own practice. The patient was operated on, apparently made a good recovery, and died two weeks later with the onset of tetanus. We had made an intestinal suture, and the autopsy which was made by Dr. LeCount or Bissell, showed tetanus organisms in the intestines and in the sutures adjacent to the bowel wall.

If the ordinary gastric and intestinal operation has this as one of its risks it is time we knew it and looked it in the face. Probably it is a risk, however slight, which no technique of preparation or operation can prevent.

DR. ROGER T. VAUGHAN: I think I can answer Dr. Lewis' question. In the clinic of Neusser in Vienna in 1907 I saw a case of local tetanus probably originating in a wound on the right foot. Both lower extremities were markedly spastic; the right more than the left, when I first saw the man, with a marked increase in the deep reflexes and with clonic spasms on percussion of the muscles. This spasticity extended from the legs up to the middle of the abdomen in the course of three or four or five days while the patient was being given daily doses of antitoxin. He never developed trismus, and this spasticity of the muscles never ascended higher than the level of the navel and, under antitoxin treatment gradually disappeared again in the reverse order of its onset. Stejskal, Neusser's first assistant at the time, made the statement that local spasticity with increase of deep reflexes, and clonic spasms on irritation is characteristic of tetanus and of no other condition. Since that time

I have been on the lookout for cases of local tetanus but have seen none, although I suppose I have observed about a score of tetanus cases of the ordinary type; but in the literature a considerable number of such cases have been reported. In only one of these cases I have seen was local spasticity a prominent feature and that was a case of right-sided head tetanus with a marked spastic facial paralysis as well as marked trismus. This patient recovered under massive doses of antitoxin. My impression is that local tetanus is a relatively mild but infrequent form of the disease. The only explanation which I can suggest for the difference between the two types of the disease is that the toxin perhaps spreads centripetally along the nerves in the local variety, but by way of the blood stream in the common variety with early trismus, and by both routes where trismus and local spasm are combined.

Dr. Kellogg Speed (closing): I desired merely to call your attention to non-traumatic, post-operative tetanus, a form which occurs after a normal, perfectly clean operation.

The case Dr. Vaughan spoke of might have had tetanic infection sometime before from the bowel or from some other source, the cryptogenic or rheumatic form, which suddenly manifested itself after the injury. I do not know of any case of two days' incubation. The cases where the spasms are localized in a limb or a group of muscles are the so-called cases of local tetanus. If you will search the literature, you will find there are hundreds reported, and recently, since the European war, a great many more are coming out in reports. I have read of several such cases in this country. I called attention to these post-operative cases because they do occur sporadically here and there and you cannot do anything for them. The first thing you know the patient has tetanus and is beyond hope. If we cannot do something in a prophylactic way in emptying the bowel or giving serum to ward off these cases, I know of nothing curative after a severe onset with a short incubation.

After my perusal of the literature and studying the subject, I can hardly believe that catgut is the cause of these infections. The case Dr. Golden cited was a very strange coincidence and it would seem to refute that idea. It may have been a sheer coincidence that the surgeon in India had tetanic infection at the same time that Dr. Murphy had such a case. I hope you will never have one of these post-operative cases because they come out of a clear sky, and in spite of best efforts the patient will nearly always die if the incubation is of short duration.

REPORT OF FOURTEEN CASES WITH ACUTE PERFORATION OF THE STOMACH AND DUODENUM, WITH END-RESULTS

Dr. C. L. Gibson, of New York City (by invitation), read a paper entitled "Report of Fourteen Cases With Acute Perforation of the Stomach and Doudenum, with End-Results." (See p. 388.)

DISCUSSION

Dr. Arthur Dean Bevan: I consider Dr. Gibson's paper a very valuable contribution to the subject of the handling of perforated gastric and duodenal ulcers. It is a clean-cut presentation of a recent group of ulcers operated on early, and certainly with remarkably good results. I agree on the whole with his conclusions.

I would like to emphasize one or two points. First, in regard to the diagnosis. Dr. Gibson states that these cases operated upon very early will give a very low mortality — possibly not more than 5 per cent. I believe that is true. The trouble has been in the past that these cases have not been operated on early, because medical men have demanded too much in the way of symptoms. The diagnosis in these cases must be made very early, and in order to make it early we must make it on a few tangible, definite facts. These are pain, muscle rigidity, and tenderness. You cannot wait to find free air in the peritoneal cavity obscuring liver dullness. I have never seen a perforating gastric or duodenal ulcer yet with that sign, although Dr. Gibson states this sign is retained in almost all the literature. You can wait for an increased leucocyte count; seen early these patients may have 8,000 or 9,000 leucocytes, and a temperature of 99°. You must make the diagnosis early, or before you can make an accurate differential diagnosis. You must accept the fact that many of these cases will be diagnosed simply as acute upper abdominal accidents without presenting data upon which to make the differentiation between an acute pancreatitis and perforating gastric or duodenal ulcer, or between a gall-bladder with perforation and acute gastric or duodenal ulcer. The diagnosis must be made with a clear understanding that it is a probable diagnosis of gastric or duodenal ulcer, but with a definite diagnosis that the patient has some acute abdominal lesion that demands an exploratory operation. I believe that if our medical men and surgeons will accept the responsibility of making these diagnoses early, much good would be accomplished but you know it requires a good deal of courage on the part of the medical man or surgeon to go into a family and urge that the patient be sent to a hospital in these early attacks and insist upon an exploratory operation, in the face of the facts that you have no data at hand that will make an absolute diagnosis for you.

In regard to the technique of management, I think Dr. Gibson is quite correct that ether is the best anæsthetic if the patient is in a fairly good physical condition and is seen early. On the other hand, I am quite convinced that a number of these patients are best operated upon under local anæsthesia, with possibly the addition during the more painful manipulation of gas carried on for a few minutes. I think morphine should be given in these cases, not as a part of the anæsthetic, but because most of these patients have an enormous amount of pain. The morphine should be given

before the operation, as soon as the operation is determined upon, for the relief of the pain before and after the operative procedure.

My own experience has been just about the same as that of Dr. Gibson in regard to the number of cases and in regard to the technique. I have found almost all of these perforations in the duodenum and in the anterior surface of the stomach. In the cases I have operated on the perforations close to the pylorus were not of large size, as a rule, and where it was possible I have used a double purse-string suture of linen or silk.

In regard to the handling of these cases so far as drainage and irrigation are concerned, I have some rather definite views. If the leakage has been small and definitely limited, I believe the best plan is to mop out the stomach or duodenal contents at that point. On the other hand, I have had several perforations that have occurred after a fairly good meal, and I think in these cases irrigation is absolutely essential, because the peritoneum does not bear very well welsh rarebit, cheese sandwiches, etc. I could not take the view that these foreign substances should be left in the peritoneal cavity because that is very bad teaching. Almost all surgeons, I think, have come to the conclusion that in the fact of gross fæcal contents, or gross stomach or intestinal contents, the peritoneal cavity should be irrigated thoroughly and in a way that will not lose any time, and this can be readily done. The peritoneal cavity in these cases should be washed out with normal salt solution, and large amounts of it at a temperature of about 108° or 110°. When it is recognized that irrigation is essential, a counter opening should be made above the symphysis, a large glass tube should be introduced and while we are putting in our purse-string sutures to close the perforation or perforations, and normal salt solution should be allowed to flow freely through the entire peritoneal cavity through the glass tube.

These cases should be drained. Dr. Gibson says he has done away with drainage. I think that is probably a good thing where there is a limited amount or no extravasation. I believe, however, where there has been gross extravasation the patient is much safer with irrigation as described and with drainage. I have worked alongside of men who have not used irrigation in these cases, and I know perfectly well my statistics and my results have been as good and better than theirs, and I am satisfied distinctly better than those men who have not irrigated in perforating cases with the escape of large quantities of stomach contents.

Just one other point in regard to the after management and it is this: In the bad cases, where drainage is necessary, many of us for years have made a mistake in using the Fowler position. A modified Fowler position is much better, the patient being kept in a recumbent position, with the head of the bed elevated about two feet, so that we obtain practically the same benefit of gravity as we do in the Fowler position without sitting the patient up.

Another thing I am much impressed with is this: Where we have a bad case, and we feel that normal salt solution by the rectum is necessary, these patients are much more comfortable with the interrupted use of normal salt solution than by the continuous use of it. Eight or ten ounces, given every two or three hours to a patient, is a very much more comfortable procedure than continuous irrigation.

In closing, I want to emphasize the fact again, that I regard Dr. Gibson's clean-cut presentation of these facts as most admirable, especially from the standpoint that he has emphasized the uselessness of gastro-enterostomy as a routine, as practiced and emphasized by Deaver and others. Think of what a foolish thing it is to advocate doing gastro-enterostomy in every case of perforation of the duodenum or perforating gastric ulcer in view of the statistics Dr. Gibson has presented tonight. There is no logical reason in the world for combining gastro-enterostomy with the operative treatment of these perforations unless there is definite evidence of pyloric obstruction. Think of the added risk of gastro-enterostomy in the face of this septic field, especially with the evidence that Dr. Gibson has presented of the curative effect apparently of the perforation and its after management in a surgical way. Personally, I feel that an important step in the after-cure of these cases is to give these patients the benefit of ulcer management. The same medical management that has proved to be so successful in the management of uncomplicated gastric and duodenal ulcer should be carried out here. I think that is true, even though Dr. Gibson's statistics are so admirable. Probably 20 per cent or more of these ulcers are multiple and because of that fact, if for nothing else, medical management becomes a very important procedure in the after-treatment.

Dr. Jacob Frank: I have been very much interested in Dr. Gibson's paper and in the results he has obtained. There is one point he has not talked about, and all the authors whose contributions I have read have not paid attention to it; namely, whether there is blood in the abdominal cavity, and in some cases where there has not been any hæmorrhage previous to the perforation.

I have a case under observation now which I operated on a little over two weeks ago in which there was a perforation near the pyloric end of the stomach large enough to introduce the thumb. It was easily recognized. The abdomen was filled with fluid. There was not the least sign of any blood in the abdominal cavity, not even in the immediate neighborhood of the perforation. No history of the patient having vomited blood previous to the operation was obtainable. The day after the operation, at which I approximated the edges of the perforation with silk and buried same with two rows of Lembert sutures, the patient began to vomit blood, and continued to do so for twenty-four hours. It was thought best to wash out his stomach. I was sur-

prised to see the amount of blood removed. I was almost afraid he was going to bleed to death, but after having his stomach washed he became comfortable and soon ceased vomiting.

In the light of this hæmatemesis I tried to reason out why it was he did not vomit before the perforation, or why there was no blood vomited at any time. The only thing I could figure out was that I must have pierced some of the blood-vessels during the inversion of the ulcer edges. I would like to know from Dr. Gibson if in any of the perforations he has encountered he has found any blood in the abdomen?

In this case I did not wash out the abdominal cavity, but I made an incision over the pubes and introduced a very large drainage tube, and also drained the site of the operation. The patient is taking solids now. There has not been any leakage in this case, although in some cases I have had leakage. It might be of interest to know in what percentage of the cases leakage occurs. I know very well that if leakage does occur, healing takes place rapidly, it being almost impossible to keep the opening patulous.

I feel as does Dr. Bevan with regard to gastro-enterostomy. I know that Dr. Deaver recommends doing gastro-enterostomy, but I have not considered myself dexterous enough, when a patient is almost moribund, to guard against more shock by doing a gastro-enterostomy. Moreover, I believe it is not necessary because all of the cases of gastric and duodenal ulcer I have had have recovered. I have in mind one case of almost fifteen years' standing, and I know of other cases of six or seven years' standing, and in not one of them has recurrence taken place. That they must be careful about their diet goes without saying.

Dr. Daniel N. Eisendrath: I would like to ask Dr. Gibson whether in any of his previous series of cases, or in his present series, he has encountered any case in which it has been impossible to close the perforation. I have encountered two such cases, one gastric, and one a duodenal perforation, in which the tissues were so indurated that all attempts to insert a purse-string or ordinary Lembert suture were of no avail, and it was necessary in the case of duodenal ulcer to suture a piece of gauze at the site of perforation. The patient recovered as though I had closed the perforation.

Dr. Bevan says that in some of his cases he would advise irrigation. Personally, I have abandoned irrigation, and I have had a relatively large number of cases of general peritonitis from appendicitis, about 60, and have had a fairly large number of cases of perforations from gastric and duodenal ulcer. I have yet to regret using the dry method, i.e., getting in and out rapidly. I think the sheet anchor which has saved a great many cases for me has been the establishment of suprapubic stab-wound drainage. That can be done in much less time than irrigation of the abdomen. As quickly as you close the perforation you place the hand above the pubes and make a stab wound, and insert a "jacket" drain down into the cul-de-sac, and place the patient up in a modified Fowler position.

I agree with Dr. Bevan in regard to the interrupted use of proctoclysis. A great many of these patients cannot stand continuous proctoclysis. I have been in the habit lately, instead of using salt solution, of using simply six ounces of tap water, with about 2 per cent bicarbonate of soda, and 2 per cent glucose, to combat the acidosis in these cases.

Dr. Gibson's X-rays are exceedingly instructive, if we can interpret the "imagination" of his radiographer; namely, that his closure of the perforation has been followed in a niche shadow in every case. His statistics are excellent, and the position he takes in regard to gastro-enterostomy is a good warning against its employment. This is dangerous in the hands of the majority of surgeons at the time of closing the perforation.

Dr. Alfred A. Strauss: I would like to speak of the additional use of fascial transplants especially in those cases where a purse-string suture is difficult to put in in cases of ulcer in which there is marked infiltration. As to the question of sepsis in connection with the fascial transplant, I would like to say that when the fascial transplant is attached with silk ligatures, instead of with catgut, the transplant becomes adherent to the tissues to which it is attached in spite of infection, and nearly all transplants which have been reported as having sloughed, if examined, will be found not to have sloughed but that the ligature has sloughed. If these fascial transplants are attached with interrupted silk sutures in every perforating ulcer, especially those cases Dr. Eisendrath referred to in which it is difficult to insert a purse-string suture on account of marked infiltrations, an additional suture certainly would do no harm.

Dr. L. L. McArthur: I would like to ask Dr. Gibson, in closing, to tell us whether he has, in view of the recent bacteriological work done on the etiological factors of these stomach ulcers, had occasion to make cultures of the secondary abscesses that occasionally complicate these perforated ulcers.

In two cases (since the work of Rosenow and others have called attention to the peculiarity of the organism), it has been my fortune to recover the fusiform bacillus as a factor in the formation of such late infections; this being one of the organisms which is accused as an etiologic factor in the formation of stomach ulcers. One of these was a late infection which perforated or extended through the diaphragm and made a septic pleurisy, and the other a subhepatic abscess, each of them containing pure cultures of the fusiform organism.

Dr. Kellogg Speed: I have operated on nine cases of perforating ulcer, one of which was carcinomatous. I take the liberty of speaking of them in order to ask Dr. Gibson a question. Of these nine cases only three recovered. The carcinoma

case died. Four cases were duodenal, and five were gastric. Two of the duodenal cases and one gastric case recovered. What struck me in the duodenal cases was the fact that the gall-bladder in two cases was markedly distended, and in addition to closing the ulcer with purse-string suture, I drained the gall-bladder and both patients recovered. In another case the gall-bladder was agglutinated over the perforation site on the pylorus and acted as a seal.

One case came into prominence. The patient or his family claimed the ulcer of the stomach resulted from a trauma. He was a working man who fell over a wheel-barrow, or was supposed to have done so, and death resulted from a perforating gastric ulcer. Under our State Compensation Act his family is now suing his employer for liability in connection with the death, and I wonder if in the discussion any one else would speak of a case where trauma was supposed to be the sole cause.

Four of my nine cases were characterized by a previous constipation. Two cases were preceded by attacks of diarrhœa occurring at least two weeks before the time of perforation, and the thought struck me, in connection with what Dr. McArthur has said, that there might possibly have been a secondary infection manifested by the diarrhœa coming into the site of the ulcer which really caused the perforation?

Dr. Sylvan Kunz: I would like to ask Dr. Gibson about how much water entered in opening the peritoneal cavity, and if there was much extravasation of stomach contents, would there not be likelihood of these contents being spread throughout the peritoneal cavity if he does not use drainage?

Dr. Wm. R. Cubbins: Doctor Gibson commented upon the fact that the liver dullness is never lost in these cases of perforating ulcer, although there is free gas in the peritoneal cavity. It seems to me that this would be explained by the intense rigidity of the abdominal muscles, which causes the costal arch to be drawn firmly down over the liver and the transverse colon. This also serves to wall the extravasated contents of the stomach or duodenum into the right hypochondriac region.

This symptom of a loss of liver dullness will occur in these cases, but as a rule it occurs only when the case is moribund, the abdomen greatly distended and the abdominal muscles paralytic. Therefore, while this is absent in an early case, it is present in a late or moribund case.

Dr. James T. Case: I have had the opportunity to examine only three cases of perforating gastric or duodenal ulcer after operation. In one of them gastro-enterostomy was done. In the other two it was not done. They all did very well. The emptying time after the gastro-enterostomy was less than three hours; in the other two it was normal.

In view of some remarks made by the speaker of the evening and several others present as to the question of the correctness of the diagnosis, I would like to say something with reference to the probability of the arrows on the roentgenograms pointing to the real site of the ulcer. In many instances it is possible to recognize definitely the actual site of the ulcer by a little projection of the gastric shadow into the crater of the ulcer. If the shadow of the stomach is seen in profile, the site of the ulcer is usually made out very well. When the ulcer is on the anterior or posterior wall, I believe it is not always possible to determine the exact location of the lesion.

One of the chief difficulties in the diagnosis of ulcer by the deformity of the gastric or duodenal shadow which it produces is the fact that a similar deformity sometimes results from adhesions. The probability of the occurrence of adhesions after operation for perforative gastric or duodenal ulcer is very great; hence, while usually in gastric, and practically always in duodenal ulcer, it is possible to show a characteristic deformity due to the ulcer. Nevertheless, in post-operative studies of patients, especially those who have been operated on for perforations, the likelihood of adhesions is very great, and I doubt if the areas indicated by the speaker's roentgenologist as shown in these slides, were always correct. We are hardly in a position to criticise this roentgenologist, for he surely did not draw his conclusions from the single plates which we have seen in the slides; probably in every case a number of plates were made.

Dr. C. L. Gibson, New York City (closing): I am very much indebted to the members of the society for their kindness and humane treatment of my paper. I am surprised there were not more objections raised, but the discussion goes to show that we are all working toward the same end. One or two things I have stated are not so much the result of my experience with this series of cases, because I have had quite a few more cases, beginning back in 1907, and the reason I did not give my whole experience was that I wanted to give the end-results in this series of cases, and since I have become connected with the New York Hospital, a period of three years, I have kept those cases in mind and have been studying them, but until I had a hospital service which I could utilize to advantage I could not do this.

As to drainage, I used to drain and wash out as Dr. Bevan does, but I had from 40 to 50 per cent mortality. Since I do not drain and wash out, I have had better results. As regards the medical management of these cases, it is only natural that we should carry it out. We treat these people with the best known therapeutic measures. I wish to say, however, that the so-called medical cures of these ulcers are fakes. You have heard Will Mayo say, and I think most of us have had the same experience, that we do not operate on these cases of chronic ulcers until they have been cured medically a number of times.

As to the question of Dr. Frank with reference to

finding blood in the abdominal cavity, I have not seen it.

With reference to the question of Dr. Eisendrath, I know there are a great many difficulties attending the closure of the perforation in some cases, but I have been spared from having an experience of that sort. When I have such a case I think I will do as Dr. Eisendrath mentioned, use a piece of gauze and sew it in, unless I adopt the suggestion of Dr. Strauss to put in a fascial transplant. I am grateful to Dr. Strauss for that suggestion, and if ever I am so unfortunate as to need it, I shall remember that valuable hint.

In regard to the remarks of Dr. McArthur concerning cultures, I have not had an opportunity to verify them. We have had trouble in only one case, and that was an elderly man with a low grade vitality, with syphilis, and who had infection of the abdominal wall. We did not make any cultures.

I cannot answer the question of Dr. Speed as regards distention of the gall-bladder, but I am grateful for the description he gives and shall bear it in mind in looking at future cases.

With reference to Dr. Kunz's question about the possibility of infecting the peritoneum by opening under water, it is a small stunt. It is not necessary in the average case, but it is a little extra resource in finding the typhoid perforation the size of a pin prick. If I had not found the cause of the case related I would have closed the incision without searching for the perforation. There was no material extravasated. The perforation was found in the cæcum. There is not much danger of carrying in infection.

CHICAGO GYNECOLOGICAL SOCIETY

REGULAR MEETING HELD DECEMBER 17, 1915, WITH THE PRESIDENT, DR. CHANNING W. BARRETT, IN THE CHAIR

CANCER OF THE UTERUS

A symposium on "Cancer of the Uterus" was presented, in which the following papers were read:

DR. THOMAS J. WATKINS, Chicago: "The Prophylaxis of Uterine Cancer," (see page 442).

DR. HOWARD C. TAYLOR, New York City (by invitation): "The Radical Operation for Carcinoma of the Uterus." This article was read also before the Clinical Congress of Surgeons, Boston, October 28, 1915 (see p. 70, January, 1916, SURGERY, GYNECOLOGY AND OBSTETRICS).

DR. DONALD C. BALFOUR, Rochester, Minnesota (by invitation): "Discussion of the Relative Merits of the Operations for Cancer of the Uterus." This paper was also read before the Clinical Congress of Surgeons, Boston, October 28, 1915 (see p. 74, January, 1916, SURGERY, GYNECOLOGY AND OBSTETRICS).

DR. C. JEFF MILLER, New Orleans, Louisiana (by invitation): "Radium in the Treatment of Uterine Cancer" (see p. 437).

DR. JAMES T. CASE, Battle Creek, Michigan (by invitation): "Roentgen Rays in the Treatment of Uterine Cancer" (see p. 429).

DISCUSSION

DR. EMIL RIES: The radical operation, as I first described it in 1895 and as I practice it today, has never been given a real trial, as far as I know, except here in Chicago. In my opinion a truly radical operation stands and falls with the thoroughness of the glandular dissection. Now, if you look through the literature or look into the operating rooms, you will find that the operators remove one or perhaps three or four glands; at any rate an insignificant number in comparison with the minimum which normal anatomy shows. If a radical operation has been performed, the internal inguinal (at least three), the external iliac (at least three), the internal iliac (at least three), the common iliac (at least two), the obturator (at least one), the sacral (at least one) glands must be shown on each side, a minimum of twenty-six (26). Who has shown them? I do not know of anybody outside Chicago. Therewith, the discussion on the radical operation may end.

The so-called radical operation which is commonly described shows very little difference from the old Freund abdominal hysterectomy, when it comes to what counts really in a radical operation, namely, the amount of tissue removed beyond the original focus. The only difference is that the ureter is more or less exposed in this so-called radical operation, while it is avoided in the old Freund operation, a difference of not more than a quarter of an inch. Anybody who exposes the ureter first instead of beginning the dissection outside the ureter and continuing it inward toward the ureter is hopelessly handicapped for a thorough glandular dissection.

My results speak favorably for the operation. All of my patients who have survived the operation and who have had a complete operation (in some cases the operation could not be completed) are well and I receive their reports annually to prove it. They were operated on in 1898, 1899, and so on down to last year. I have lost track of the first case (operated on in 1896) ten years after the operation, when she last reported. The operative mortality is high, around 25 per cent; but I have oper-

ated sometimes where the conditions were not favorable.

I had hoped that the treatment of carcinoma of the cervix with radio-active substances would fulfill the promises it gave, but I have been unable to see in this country any demonstration of results such as our European confrères have published. All the cases which I have turned over to the specialists in X-ray and mesothorium treatment are worse than when they started treatment, or dead. In the absence of clinical demonstration of cure by the radio-active substances, I wish to emphasize what Dr. Miller has brought out and what ought to be remembered when we look at the pretty pictures of cancer influenced by radio-active substances. Degenerated areas of cancer-cells prove nothing at all, for first of all every cancer shows degenerating areas along with its devastating progress; and secondly the complete destruction of more or less superficial areas after the radio-active treatment proves nothing whatever as to what is going on in the depth. And in the cases which I have seen, progress in the depth has been the steady companion of the deceptive superficial effect.

DR. KOLISCHER: I have nothing to add to Dr. Ries' remarks about the abdominal radical operation. As to the employment of the actual cautery in cancer of the uterus, I would like to say this: one is justified in being rather doubtful as to the efficiency of this attempt at reviving this abandoned method. First, the extension of the heat in the depth beyond the area of application is rather limited, as one may readily convince oneself by testing the penetrating power of a Paquelin tip or of a soldering-iron on a piece of meat; secondly, medical history furnishes strong arguments against the value of this method. Mackenrodt, for instance, dissatisfied with the vaginal hysterectomy for cancer, about twenty years ago used the actual cautery; first the Paquelin and then the soldering-irons for this purpose. After a prolonged trial he discarded this procedure in favor of the abdominal operation. If one really desires to coagulate tissues to any appreciable depth, diathermy has to be employed, which method permits of extending the coagulation to any desired depth. I am very much pleased with the conservativism displayed by Dr. Case in regard to the efficiency of X-rays in uterine cancer. In a general way, I would like to remark that reports on the therapeutic value of the X-rays must be based on certain principal premises. Efficacy of the apparatus and completeness and reliability of the measuring outfit are paramount among these. The conviction that photometric tests are of little value in judging the therapeutic force of rays is constantly gaining followers.

The efficiency of the tube depends on its hardness, its constancy, and the quantity of usable rays produced. To measure the latter is only possible by the iontometer. It may not be amiss to mention on this occasion that the Coolidge tube, so enthusiastically hailed when put on the market, is rather severely criticized by some physicists as to its therapeutic value, on the ground that it cannot be sufficiently raised, and if raised to its limit, about eight Bauer, does not permit of a sufficient amperage.

That tubes that are cooled by running ice-water invariably can be raised beyond ten Bauer under 5 milliampere pressure and kept there during several hours of action can be demonstrated to anyone who would take the trouble of visiting the Radiotherapeutic Department of the Michael Reese Hospital.

As to the employment of radio-active substances I will have to admit that out of 57 cases of uterine cancer of various descriptions I am able to report only on 2 cases as successes; that is, both cases were inoperable cancers of the cervix, and in one after eleven, in the other after nine months' time, I am unable to find any evidence of disease. In the case mentioned by Ries, while locally epithelialization took place under mesothorium, at the left side of the portio a crater formed penetrating the parametrium. Ries lately cleaned that out and mesothorium was introduced into the cavity. I intend later to repeat this application. I do not expect a result in this case.

Judging from the reports coming from Europe concerning the mesothorium treatment of uterine cancers, and I have no reason to doubt statements made by men like Kroenig, Klein, Doederlein, Bumm, etc., I feel convinced that the superiority of their result is due to their refined technique which we must endeavor to acquire.

In conclusion I would like to mention that the overwhelming majority of these reports is based on the use of mesothorium and not of radium, the latter having been practically abandoned in favor of mesothorium.

BOOK REVIEWS

A CRITIQUE OF NEW BOOKS IN SURGERY

By MAJOR G. SEELIG, M. D., St. Louis

PERHAPS it is referable to the European war and perhaps not, but surely there is a notably evident quantitative depreciation in medical books. Furthermore, perhaps this quantitative falling off is a good omen, signifying healthy continence, or perhaps an ill omen significant of the paralytic influence of Mars. At all events, the truth of the matter is that during the course of the past two or three months the entire output of surgical volumes would not constitute a corporal's guard in even the most neutral of libraries. If the war is really the moving cause of the scarcity, and if men are not thinking or writing (surgically of course) because they are too busy fighting and dying, then one fearingly hesitates to contemplate the deluge of pent up literature that will overwhelm us after peace is declared, and the flood gates of publication are reopened.

One is almost tempted to wish that instead of being obliged to contribute set reviews of definite and very concrete volumes, he might allow himself the liberty that that most excellent of literary reviewers, Francis Hackett, grants to himself. Mr. Hackett heads his department in *The New Republic*, "Books and Things," thereby relieving himself of all necessity of confining his comment to any special volumes. Unfortunately, however, the medical reviewer may neither grant to himself nor have granted to him license or latitude. He must, perforce, do just as I am obliged to do this month, start off by saying that four books will be reviewed —all of them, by the way, command unusual interest—one of them purely surgical, one of them roentgenological, and one of them autobiographical.

The purely surgical volume deals with the very recently developed and still developing field of bone grafts;[1] and never was the appearance of a volume better timed. We are right now in a period of renaissance of bone surgery, and we are in need of just the kind of volume that Dr. Albee has written; namely, one that deals with the fundamental principles underlying bone grafting, the specialized technique of making and inserting the grafts, and the consideration of when and where to use the grafts. The book is made up of eight chapters devoted to the fundamental principles underlying the use of the bone graft in surgery, the author's electric motor operating outfit and technique of usage, the bone graft in the treatment of Pott's disease and other lesions of the spine, the inlay bone graft in the operative treatment of fractures, operative measures for remodeling or ankylosing the hip joint, the inlay bone graft for fixation of tuberculous knee joints, infantile paralysis, osteoarthropathy (Charcot's disease), the wedge graft for habitual dislocation of the patella, the bone graft in the treatment of diseases and deformities of the foot and leg, and miscellaneous surgical uses of the bone graft.

An adequate book review should be not only explanatory and critical, but also informative; that is, it should furnish the reader with information stimulated by the volume under discussion, but not contained in it. One cannot be informative in this sense of the word, in reviewing Albee's book, for he has embraced between both covers about all the information that has been furnished us by current literature. He has done this, moreover, in an admirably terse and concrete fashion. In the short space of thirty-five pages he outlines the historical development of the subject of bone grafting, the histological principles underlying bone grafting, the nature of homoplastic, autoplastic, and heteroplastic grafts, the bearing of Wolff's law on the growth of bone grafts, the rôle of the periosteum, various methods of preservation of bone grafts, and finally a tabulated list of all the indications for the use of bone grafts. It is interesting to note that Albee considers only two valid contra-indications to the insertion of bone grafts; namely, a markedly septic field of operation, and extensive scar-tissue as an environment.

The first chapter, in which all the above subjects are touched upon, is a remarkably good example of lucid, expository writing. On page thirty, the author succeeds in emphasizing all the elements essential to successful grafting in one not unduly long paragraph. He has a way of setting his reader right that is well illustrated by his forceful introduction of the subhead, "The Rôle of the Periosteum," which he opens with a sentence emphasizing the osteogenetic nature of the periosteum and leads from this to the advice that "every graft should have as large a covering of periosteum as possible."

[1] Bone-Graft Surgery. By Fred H. Albee, A.B., M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Company, 1915.

All his conclusions are stated with about this same degree of definiteness and yet, as a rule, without dogmatism; and there is throughout a healthful respect for the opinions and labors of other investigators. In a volume of this high character it would probably not have been amiss to have appended a complete bibliographic chapter, as a supplement to the many references furnished in the text.

The seven succeeding chapters are largely technical in character and constitute a practical *vade mecum* to the operating surgeon. The fact that the methods described are, all of them, Albee's methods does not constitute a disadvantage, but rather furnishes that personal note of value indispensable in this type of book. To have dilated upon variations of method would have made the volume much less readable, and much less valuable, though possibly more encyclopædic in scope. No book was ever better illustrated or furnished better evidence of a real appreciation of the type of sketch necessary to illustrate steps in technique.

NOW and then, in the past, it has been necessary to call a consultation in order to do full credit to a volume of borderland surgical significance. Once again we resort to a special court, and submit the following judgment by Dr. R. Walter Mills, on the volume by George and Leonard[1] (*Roentgen Diagnosis of Surgical Lesions of the Gastro-intestinal Tract*) and the short review, by Dr. Clifford G. Grulee, on the latest volume of the *Reference Handbook of the Medical Sciences:*

"The very great interest at present evinced in gastro-intestinal surgical radiology finds its first American expression in textbook form in a combined textbook-atlas volume by George and Leonard. The authors are to be congratulated on their courage in attempting to submit a view of a field so rapidly extending its boundaries. Where so many ideas and methods are striving for precedent in the construction of a subject, it is not surprising that the authors advocate with unqualified abandon one system of gastro-intestinal radiology, in this case that of a modified serial plate method. The entire volume finds its motif in the enthusiasm of the authors for this method to the prejudice of the time-honored radioscopic or combination radioscopic and plate methods. The strength of the book, also its weakness, lies in this. It is not difficult to trace the origin of this position to a development from Cole's original teachings of a practical and exceedingly valuable method of plate diagnosis of the majority of duodenal ulcers, a method that has been developed through the work of the authors and their co-workers. Extreme partisanship for this plate method leads the authors to statements that are both very radical and not altogether unassailable. For instance, that the roentgenographic method alone serves to show defects and that 'the continental school is based on a somewhat uncertain combination of clinical symptoms and varied roentgenoscopic manifestations of motility.' This statement is made in spite of the fact that the filling defects of gastric carcinoma, the evidence of penetrating and callous ulcer, and of the form and position of the stomach in cases of pyloric obstruction and the like, originated in the roentgenoscopic method. Again the statement in the preface to the effect that the authors have 'found the clinical evidence to be so superficial and inaccurate, that they have practically eliminated from the text the whole clinical story' is certainly an extreme position when one considers the peculiarly characteristic anamnesis of duodenal ulcer, œsophageal carcinoma, colonic obstruction, and similar lesions. At least it might be anticipated that the authors would acknowledge the value of clinical findings as of economic importance in directing their roentgenological efforts. Another position that will not be supported by a very considerable number of radiologists is the valuelessness of the six-hour residue as an indication of impaired gastric motility. Such evidence is contrary to the experience of workers of high standing, basing their observations on a study of a large material, and using practically the same opaque media as the authors. This discrepancy, it may be suggested, is possibly due to the fact that George and Leonard examine their cases when not absolutely fasting and allow a 'light meal' during the interim between the initial and the six-hour observation.

"On the other hand, the volume is of exceptional worth in presenting the value to be derived from a careful consideration of properly exposed plates, from intelligently posed patients, in considerable numbers. The work will make a strong appeal to those who have questioned the value of gastro-intestinal radiology, and to those who are not informed as to its accomplishments; and it will do this because all conclusions are reached from a consideration of X-ray findings alone; possibly this is not the means of utilizing most fully the possibilities of the X-ray in diagnosis, but nevertheless it is a method that makes a powerful argument. The chapter on radioscopy of duodenal ulcer marks a new epoch. In the chapter on the X-ray diagnosis of gall-stones the authors again take an extreme position as to the diagnostic effectiveness of special plate technique and inspection. Their optimism is not shared by many other workers.

"The conscientious citation of operative findings in practically all cases, with due appreciation of those not so confirmed, and the comparison of such data with the original X-ray conclusions is most gratifying. The book is beautifully printed and is illustrated profusely with positive reproductions of roentgenograms very evidently selected from a considerable material. The roentgenograms are mostly of admirable quality; it is to be regretted that the water-colors and tone drawings hardly attain the same excellence."

[1] THE ROENTGEN DIAGNOSIS OF SURGICAL LESIONS OF THE GASTRO-INTESTINAL TRACT. By Arial W. George, M.D., and Ralph D. Leonard, A.B., M.D. Boston: The Colonial Press, 1915.

"THIS[1] continues a most useful set of books. Practically everything in medicine is covered. In this particular volume, the article on lymphatics and lymph-nodes is specially worked up in detail with some very good illustrations. The lymphatics of all the different organs are minutely described and shown. There is a long article with list of instruments on mastoid operation. Medical Licensing Boards and Medical History come in for their share. Other conditions are handled with much the same degree of completeness."

THERE may be, in the minds of some, a very legitimate doubt regarding the appropriateness of including an autobiography, and a non-surgical autobiography at that, in the book review columns of a purely surgical journal. But it has always seemed that surgery as a science should correspond to that most admirable definition of science furnished by President Hadley, who said: "Science is not a department of life which may be partitioned off from other parts; it is not the knowledge of certain kinds of facts and the observation of certain kinds of interests, as distinct from other facts and other interests; it is a way of looking at life and dealing with life; a way of finding out facts of every kind and dealing with interests as varied as the world itself:

"Where each for the joy of working, and each in his separate star,
Shall draw the thing as he sees it, for the God of things as they are."

If we agree to accept this broad definition, then we may brave all caviling and say just enough about this autobiography by Trudeau[1] to make every one of our readers experience the inner need of reading it. I know of no other medical autobiography just like it; this is essentially so because Trudeau (as he says in his foreword) "has drawed his soul"—a soul picture as distinguished from a man picture—and no approximate counterpart to Trudeau's soul has ever lived in human body.

Never was there a more poignant expression of the doctrine of fate conquered by acquiescence, never a more modest or more detached recital of a really great achievement against withering odds, never a more infectious breathing of the love of out-of-doors, of family, and of friends. The book fairly radiates the doctrine of loss of self in an effort of high purpose, and teaches the lesson of optimism in such pervasively subtle fashion as to clutch the heart of even the casual reader. There are no swashbuckling preachments on happiness at any cost, none of the usual dogmas of *per aspera ad astra*, but just a simple, straightforward, touching recital of hopes, struggles, buffets, joys, and victories. No man may read the book and fail to face his own daily problems with calmer spirit and saner determination.

[1] A Reference Handbook of the Medical Sciences Embracing the Entire Range of Scientific and Practical Medicine and Allied Science. By various writers. Third edition, completely revised and rewritten. Edited by Thomas Lathrop Stedman, A.M., M.D. Eight volumes. Vol. VI, Lig-Oza. New York: William Wood & Co., 1916

[1] An Autobiography. By Edward Livingston Trudeau, M.D. Philadelphia and New York: Lea & Febiger, 1915.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

A Treatise on the Principles and Practice of Medicine. By Arthur E. Edwards, A.M., M.D. Philadelphia and New York: Lea & Febiger, 1916.

Obstetrics—A Practical Textbook for Students and Practitioners. By Edwin Bradford Cragin, A.B., A.M. (Hon.), M.D., F.A.C.S. Assisted by George H. Ryder, A.B., M.D. Philadelphia and New York: Lea & Febiger, 1916.

A Textbook of Nervous Diseases. For students and practicing physicians; in thirty lectures. By Robert Bing, Dozent of Neurology, University of Basel. Translated by Charles L. Allen, M. D., New York: Rebman Company, 1916.

With the Red Cross in France; the Aftermath of Battle. By Edward D. Toland. New York: The Macmillan Company, 1916.

Surgical Operations with Local Anesthesia. By Arthur E. Hertzler, A.M., M.D., Ph.D., F.A.C.S. Second edition. New York: Surgery Publishing Company, 1916.

The Medical Clinics of Chicago. January 1916. Philadelphia and London: W. B. Saunders Company, 1916.

Post-Mortem Examinations. By William S. Wadsworth, M.D. Philadelphia and London: W. B. Saunders Company, 1915.

Bandaging. By A. D. Whiting, M.D. Philadelphia and London: W. B. Saunders Company, 1915.

The Clinics of John B. Murphy, M.D., at Mercy Hospital, Chicago. December 1915, IV, No. 6. Philadelphia and London: W. B. Saunders Company.

Nitro by Hypo; a Peptonized Tonic for the Physician. By Edwin P. Haworth. Kansas City, Missouri: The Willows Magazine Company.

Roadside Glimpses of the Great War. By Arthur Sweetser. New York: The Macmillan Company, 1916.